Sclerotherapy emergencies & complications
Eric Mowatt-Larssen, MD, FACPh, RPhS
Monterey, California

Conflict of interest
• Foam sclerotherapy is an off label use of an FDA approved medication

Severe complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Liquid</th>
<th>Foam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaphylaxis</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
</tr>
<tr>
<td>Large tissue necrosis</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
</tr>
<tr>
<td>Motor nerve injury</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
</tr>
<tr>
<td>PE</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
</tr>
<tr>
<td>Proximal DVT</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
</tr>
<tr>
<td>Distal DVT</td>
<td>0.01 - 0.1%</td>
<td>0.1 - 1.0%</td>
</tr>
</tbody>
</table>

Rabe, European consensus, Phlebology 2013
### Minor complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Liquid</th>
<th>Foam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matting</td>
<td>1 – 10%</td>
<td>1 – 10%</td>
</tr>
<tr>
<td>Residual pigmentation</td>
<td>1 – 10%</td>
<td>1 – 10%</td>
</tr>
<tr>
<td>Visual disturbances</td>
<td>&lt;0.01%</td>
<td>0.1 – 1%</td>
</tr>
<tr>
<td>Headaches or migraine</td>
<td>&lt;0.01%</td>
<td>0.1 – 1%</td>
</tr>
<tr>
<td>Sensory nerve injury</td>
<td>0</td>
<td>0.01 – 0.1%</td>
</tr>
<tr>
<td>Skin necrosis (mild)</td>
<td>0.01 – 0.1%</td>
<td>&lt;0.01%</td>
</tr>
<tr>
<td>Embolia cutis medicamentosa</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
</tr>
<tr>
<td>Chest tightness</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
</tr>
<tr>
<td>Dry cough</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
</tr>
<tr>
<td>Localized allergy</td>
<td>&lt;0.01%</td>
<td>&lt;0.01%</td>
</tr>
<tr>
<td>SVT</td>
<td>Unclear</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

Rabe, European consensus, Phlebology 2013

### Agenda

- Anaphylaxis
- Stroke
- Arterial injection
- Hyperpigmentation
- Matting

### Case

- 62 yof with symptomatic anterolateral thigh VV
- "Mild asthma", allergies to pollen & perfume, NKDA
- #1 – UGFS STSF 3%, 4 mL
- #2 – 6 months later, UGFS STSF 1%, 12 mL

Scurr, EJVES 2007
Course

- 20 min later, tongue and lips feel "hot"
- Exam – facial flushing -> chlorphenamine (H1-blocker) 10 mg IV
- HR 120, BP 79/50, wheezes, tongue & lip edema -> O2, epi 0.5 mg IM, IVF, hydrocortisone 100 mg IV
- Observed 24 hours & discharged

Emergency resuscitation equipment should be immediately available. Allergic reactions, including fatal anaphylaxis, have been reported. As a precaution, the following steps should be taken in case of anaphylaxis:

- Skin or mucosa*: generalized hives, pruritis, flushing, swollen lips-tongue-uvula
- Respiratory (SOB, wheeze, stridor, hypoxia)
- Vascular (hypotension, syncope, incontinence)
- Gastrointestinal (persistent abdominal pain, vomiting)

Sampson, Second Symposium, AEM 2006
Table 3. Differential findings in anaphylaxis versus vasovagal reaction.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Anaphylaxis</th>
<th>Vasovagal Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms onset</td>
<td>Sudden onset</td>
<td>Protracted onset</td>
</tr>
<tr>
<td>Skin</td>
<td>Rash (urticaria, angioedema)</td>
<td>Cool and clammy</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Wheezing, cough, or respiratory distress</td>
<td>Normal</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Tachycardia, palpitations</td>
<td>Hypotension</td>
</tr>
<tr>
<td></td>
<td>Bradycardia, arrhythmia</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Anxiety or impairment of consciousness</td>
<td>Lightheadedness, syncope, irritability</td>
</tr>
<tr>
<td></td>
<td>Dizziness, blurred vision</td>
<td>Nausea</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Vomiting or diarrhea</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Mowatt-Larssen, Phlebology 2013

Pathophysiology

Simons, J Allergy Clin Immunol, 2009

Prevention – sclerosants

- No cross reactivity between polidocanol and sodium tetradecyl sulfate
- Sodium tetradecyl sulfate – sulfa allergy not a contraindication
Prevention – local anesthetics

- Lidocaine
- Mepivacaine
- Dibucaine
- Procaine
- Cocaine
- Benzocaine
- Pontocaine

Amides | Esters

Urgent actions

- ABCs
- **Epinephrine** intramuscular
- Early intubation if airway obstruction
- Albuterol if wheezing
- Fluid resuscitation, IV lock
- Oxygen

Epinephrine: the drug of choice for anaphylaxis. A statement of the World Allergy Organization

Allergy 2008

Epinephrine

- 0.5 mg IM to anterolateral mid–thigh
- Every 5 minutes if needed
- Relative contraindications – CAD, dysrhythmias, elderly, pregnant
- Adverse effects – anxiety, pallor, tremor, palpitations, dizziness, headache

Simons, J Allergy Clin Immunol 2009
Other treatments

- H1-blockers – diphenhydramine 50 mg IV – slow onset, effective for itch and hives
- H2-blockers – famotidine 20 mg IV
- Corticosteroids – prevent protracted or biphasic symptoms

Monitoring & follow up

- Vital signs are vital
- Biphasic reaction – up to 72 hours later
- Corticosteroids may prevent biphasic reaction
- Epipen prescription
- Consider Allergy consult

Table 6. Common errors in the management of anaphylaxis.

- Missing the diagnosis (e.g., not undressing the patient to look for urticaria)
- Missing an upper airway obstruction (makes subsequent airway intubation difficult)
- Not using epinephrine (highly recommended in most patients with severe urticaria; respiratory symptoms or signs; or cardiovascular symptoms or signs)
- Inadequate intravenous fluid resuscitation (patients may require multiple liters)
- Biphasic reaction (monitor the patient after symptoms clear and discuss this possibility with the patient)

Mowatt-Larssen, Phlebology 2013
Case
- 61 yom, CEAP C4, SFJ + GSV reflux
- PMHx DM, htn, dyslipidemia, asthma, migraine without aura
- UGFS POLF 0.5%, 20 mL, SFJ compressed
- While dressing, RUE weakness & frontal headache & sweating
- Exam – mild expressive aphasia, Strength RUE 1/5 & RLE 4/5, decreased vibration bilateral, CN intact

Forlee, JVS 2006

Course
- 10 min later, Strength RUE improves to 4/5
- Immediate carotid Duplex shows normal arteries, foam particles left carotid
- MRI brain normal
- Telemetry NSR
- Echo PFO 18 mm, R->L shunt
- Over 2 weeks, fine motor function mildly impaired, gross strength normalizes
Risks – acute neurological symptoms

- Can occur after:
  - Foam sclerotherapy (1)
  - Liquid sclerotherapy (2)
  - Thermal ablation (3)
  - High ligation & stripping (4)
  - Phlebectomy (5)

1. Forlee, JVS 2006
3. Caggiati, CVA after EVLA, JVS 2010
5. Passierello, Phlebology 2011

Pathophysiology

- Migraine +/- aura (endothelin 1)
- Arterial gas embolism (bubbles)
- Paradoxical thromboembolism

TIA vs. migraine with aura

- 20 patients (11 clinics) with visual disturbances after foam sclerotherapy
- Occur @ average 7.4 +/- 6.5 (range 0.5–30) min after end of injections
- Usually < 30 min duration (max 3h)
- 25% LE paresthesias, 10% tongue paresthesias
- 5% dysphasia, 50% headache
- 75% h/o migraine
- All symptoms fully reversible

Gillet, Phlebology 2010
Migraine & aura

- Neurologist analyzed form information
- Diffusion-weighted MRI read by neuroradiologist within 2 weeks (15/20) or late (3/20), all normal
- All were migraine with aura, not TIA
- Endothelin (vasoconstrictor) release thought the etiology

Arterial gas embolism

- 72 yof
- UGFS STS 2 x 2 mL calf perforators
- 25 min later, slumped in chair, slurred speech, L>R weakness
- CT - air in vertebral artery
- @ 3 hours, symptoms resolve

Bush, Phlebology 2007

Paradoxical gas embolism

- Requires R→L shunt + R>L pressure
- Or large gas bolus (>20 mL) or continuous gas (>11 mL/min) in animal studies
- Then bubble occludes arteriole or artery
- And causes inflammatory response

Muth, NEJM 2000
Right to left shunts

- Patent foramen ovale – 25-35%
- Pulmonary arteriovenous malformations – 10%
- PFO in migraine patients – 60%

Oxygen establishes diffusion gradient favoring egress of gas from bubbles
- Flat supine position – head-down may aggravate cerebral edema
- Hyperbaric oxygen reduces bubble size and creates tissue hyperoxemia and may reduce cerebral edema (reduce blood vessel permeability)
- Normovolemia

Paradoxical thromboembolism

- 56 yof, UGS STSF 16 mL, enoxaparin 40 mg
- @ 2 days, L weakness & dysphasia
- R MCA CVA, MRI no bubbles
- Complete recovery 1 hr later
- DUS non-occlusive DVT MGV -> pop
- PFO 25 mm
- Normal carotid & vertebral arteries
PTE treatment

- Probably a significant cause of cryptogenic stroke (CS)
- PFO detected in 40–50% of CS
- But recurrent CVA risk not higher in patients with PFO + CS
- PFO closure is controversial

Prevention

- We cannot prevent bubble migration (1)
- Minimize bubble size? – inspection, turn stopcock 30°, filter, manufactured foam
- Limit volumes? – total to <10 mL or per injection volumes to <0.5 mL?
- CO2/O2 vs. air?

Urgent actions

- Oxygen
- Complete and repeated neurological exams
- Mild visual or sensory symptoms which clear -> likely migraine/aura
- Motor symptoms or persistent symptoms -> emergency department

1 Morrison, Phleology 2009

Finsterer, Acta Neurol Belg 2010
Case
- 43 yom symptomatic VV
- Ankle -> groin stripping
- @ 6 weeks, STS 3% to medial ankle varix
- Immediate pain, foot blanching, dysesthesias
- Arteriography shows PTA spasm without occlusion
- Catheter IV NTG & papaverine & UFH
- Lateral plantar artery tissue necrosis

Bergan, Derm Surg 2000

Arterial injection – diagnosis
- Pain
- Pallor -> mottling & cyanosis
- Paresthesias -> anesthesia
- Weakness -> Paralysis
- Poikilothermia
- Pulselessness
- Skin and fat necrosis
Differential diagnosis

- Sclerosant extravasation – bright erythema or blistering -> dilute with hyaluronidase
- Reactive vasospasm – immediate porcelain-white appearance -> nitroglycerin 2%

Arterial injection pathophysiology

- Denatures blood & endothelial cells
- Sludge embolus**
- Obstructs microcirculation
- Arteriospasm**
- Skin, nerve, muscle necrosis

Goldman, Complications and Adverse Sequelae of Sclerotherapy, In Sclerotherapy, 4th Ed., 2007

Modern episodes

- 5 cases
- Experienced phlebologists
- Correct procedures
- Sclerosant visualized intravenous on ultrasound

Bergan, Derm Surg 2000
Prevention

- Ultrasound guidance!
- Higher risk anatomy – perforators & joints (medial malleolus, popliteal fossa, groin)
- Low pressure blood return from needle
- Low syringe pressure

Treatment

- Coordinate with urgent vascular surgery consult
- Heparin – anti-thrombotic
- Nitropaste local application – vasodilator
- Lidocaine injection – vasodilator & analgesic
- Catheter-guided thrombolytics
Hyperpigmentation

- Brown skin staining in an area of recent sclerotherapy
- RBC extravasation followed by hemosiderin-laden macrophages -> hemosiderin tattoo

Matting

- New telangiectasias in an area of previous sclerotherapy
- Pathophysiology – angiogenesis

Preventing hyperpigmentation & matting

- Minocycline & iron (hyperpigmentation)
- Estrogen (matting)
- Treat reflux proximal to distal (minimize venous hypertension)
- Minimize sclerosant concentration (inflammation -> RBC extravasation or angiogenesis)
- Minimize injection pressure (direct RBC extravasation or wall damage)
- Compression stockings post-procedure
Hyperpigmentation

- Drain trapped blood
- Usually resolves with time (months to a year)
- Persistent hyperpigmentation - laser (Q-switched)

Matting

- Gentle sclerotherapy (small needles, low sclerosant concentrations)
- Usually resolves with time (months to a year)
- Persistent matting - laser (532 nm, PDL)

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Medicine is a team sport

- Rehearse actions that improve patient outcomes - mental & physical
- Plan for an emergency - assume the worst, hope for the best
- Understand pathophysiology - weak data
Resuscitation equipment

- Oxygen
- AED
- Medications – epinephrine, diphenhydramine, methylprednisolone, aspirin
- Emergency cart/kit

IAC Vein Center Accreditation, 2015

Sclerosants & the FDA

- FDA approved – STS, polidocanol, HT saline, glycerin, sodium morrhuate
- Foaming is an off-label use of an FDA-approved medicine

Morrison, "Chemical superficial vein ablation", in EML et al. (eds), Phlebology, Vein Surgery and Ultrasonography, 2014

Compounded or imported sclerosants

- Sclerosant concentration inaccuracies
- Presence of impurities
- Possible fraud (Medicare or insurance carrier policies)

Morrison, "Chemical superficial vein ablation", in EML et al. (eds), Phlebology, Vein Surgery and Ultrasonography, 2014
Low risk procedure considerations

- Discuss “multiple allergies” and “asthma”
- Known symptomatic right to left shunt
- Avoid foam for neurological symptoms from previous treatment
- Use ultrasound guidance
- Small foam bubbles
- Avoid high volumes such as >10mL/day or >0.5/injection
- Avoid high pressure injections
- Avoid Valsalva immediately after treatment

Conclusions

- Inform patients about possible serious adverse events during consent
- Know how to diagnose and manage serious adverse events
- Inform patients about foaming being off label
- Implement low risk protocols to minimize risk