Sclerotherapy emergencies & complications

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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
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

Severe allergic reactions have been reported following polidocanol use, including anaphylactic reactions, some of them fatal. Severe reactions are more frequent with use of larger volumes (> 3 mL). The dose of polidocanol should therefore be minimized. Be prepared to treat anaphylaxis appropriately.

Prescribing instructions for STS & POL
Diagnosis – anaphylaxis

- Two or more systems:
  - **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>
<thead>
<tr>
<th>Variable</th>
<th>Anaphylaxis</th>
<th>Vasovagal reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom onset</td>
<td>Sudden onset usually</td>
<td>Prodrome usually</td>
</tr>
<tr>
<td>Skin</td>
<td>Rash (erythema, urticaria, angioedema)</td>
<td>Cool and clammy</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Wheezes, stridor or respiratory distress</td>
<td>Normal</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Tachycardia, prolonged hypotension</td>
<td>Bradycardia, transient hypotension</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Anxiety, no improvement despite supine positioning, sense of impending doom</td>
<td>Lightheaded, syncope, improves with supine positioning</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Vomiting or diarrhea</td>
<td>Nausea</td>
</tr>
</tbody>
</table>

Mowatt-Larssen, Phlebology 2013
Pathophysiology

IMMUNOLOGIC: IgE/FceRI
- foods
- medications
  - eg β-lactam antibiotics
- insect stings/bites
- natural rubber latex
- other

IMMUNOLOGIC: OTHER
- IgG-antigen complexes
- complement system activation
- coagulation system activation

NON-IMMUNOLOGIC
- exercise
- cold air or water
- medications, eg. opioids
- other

CELLS
- MAST CELLS
- BASOPHILS

MEDIATORS
- PREFORMED
  - HISTAMINE
  - TRYPTASE
  - CARBOXYPEPTIDASE A
  - CHYMASE
- NEWLY GENERATED
  - LEUKOTRIENES
  - PROSTAGLANDINS
  - PLATELET-ACTIVATING FACTOR
- OTHER
  - CYTOKINES
  - CHEMOKINES

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)
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
2 Hanisch, CVA after liquid sclero, Eur J Med Res 2004
3 Caggiati, CVA after EVLA, JVS 2010
4 Harzheim, CVA after surgery, Dtsch Med Wochenschr 2000
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%
PGE treatment

- **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)
- Normovolemic
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

Ma, Phlebology 2011
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

Finsterer, Acta Neurol Belg 2010
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?

1 Morrison, Phleology 2009
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
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

Early

Late
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*

Courtesy J Mauriello
Matting

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

Courtesy H Fronek
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
Treatment

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

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

- *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