Sensory Neuropathic Cough

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For voice, swallowing, and airway disorders

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Anecdote 1

- Supraglottic laryngectomy patient—now 4 y. postop
- At routine CA f/u visit, diagnosed herpes zoster oticus
- Next visit, (4 M later) had developed post-herpetic *neuralgia*
- *On **amitriptyline***

Anecdote 2

- ~80 y.o. obese woman – poor historian—c/o "dry patch" during the past 6 months
- "Oh Doctor, *when it happens*, I just *jump up* and ***run*** to the kitchen for a drink . . ."
- Points to side of neck
- Seems instantaneous, neuralgia-like
- On a hunch you try amitriptyline . . . And it works!

Anecdote 3

- ~40 year old electrician, "Clint Eastwood type"
- CC: "I'm gagging."
- "I gag if I touch my neck; I can't button my collar . . ."
- You ask: "Lifelong?" He replies, "6 months."
- *You ask: "May I touch your neck?"* (GAG!) . . ."
- Trigger phenomenon seems neuralgia-like
- On a hunch, amitriptyline, → response!

Anecdote 4

- Chronic Cough, for years, in middle-aged woman (like dozens before her . . .)
- No response to RX for GERD, asthma, allergy, antibiotics
- Major workup has been negative
- Coughing caused by sudden tickle triggered by talking and …
- She responds to amitriptyline!

SNC: The concept . . .

- If one can have neuropathic PAIN or *neuralgia,* then why not
  - Neuropathic tickle
  - Neuropathic "dry sensation"
  - Neuropathic "sandpaper"
  - Neuropathic "pins and needles"
  - Neuropathic "mucus" etc.

And why couldn't they → cough?

SNC: What it ISN'T. . .

- Cough-variant asthma, GERD, or Psychogenic coughing
  - Different history
  - Different cough "phenomenology"
  - Different test results
  - Different response to RX

In Particular: Must be able to recognize nonorganic cough

- Young women
- Stereotyped cough pattern
- Perfunctory ("unconvincing")
- Distractable
- *La belle indifference*
- May be episodic
- Psychogenic, not *neurogenic*

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Sensory Disturbance: Terminology

- **Neuralgia**: acute spasmodic pain along the course of one or more nerves → "Cough neuralgia"
- **Dysesthesia**: a) Impairment of sensation, or a disagreeable one produced by ordinary stimuli or no stimulation → "Cough dysesthesia"
- **Paresthesia**: abnormal sensations (as tingling or tickling or itching or burning) usually associated with peripheral nerve damage → **"Cough paresthesia"**
- **Neuropathy**: any disease of cranial or peripheral nerves→ **"Sensory Neuropathic Cough" or just "neurogenic cough"**

Related Syndromes to which Otolaryngologists Can Relate

- Trigeminal Neuralgia
- Glossopharyngeal Neuralgia
- Laryngospasm – esp. with VF paralysis (often starts with tickle or cough) More, later . .
- Post-herpetic neuralgia in H/N
- **….VAGAL neuralgia / paresthesia / dysesthesia? Let's describe it . . .**

Intractable Coughing in our Practices: Response to Prior Treatments

- PPI's: NR
- Asthma inhalers, both steroid and bronchodilator: NR, or triggers cough
- Cough Suppressants: NR*
- Antibiotics: NR or brief benefit
- Steroids: NR or brief benefit

Description of the Cough Itself: Severe episodes

- Sudden tickle, commonest @ sternal notch
- **Aggressive** coughing at least at times (+/- laryngospasm)
- Oculo- and rhino-rrhea
- 10 sec to 5" duration
- May throw up, have urinary incontinence break ribs, develop subconjunctival hemorrhage

Description of the Cough cont'd
Severe episodes

- Strangers offer water
- Heimlich maneuver
- Make "scene" in public—must leave
- Humiliating!

Audio / Video Clips

- 1. Description of sensation

- 2. Moderately-severe attack

A couple of caveats in history-taking

- Patient unfamiliarity a hindrance
- When told "my cough is productive," press the patient
  - Something comes up first few coughs?
  - (Or, does bronchorrhea coincide with or follow oculo- and rhinorrhea?)

In other words, ask yourself and patient, is bronchial secretion the <u>result</u>, rather than the <u>cause</u> of the cough?

"Neuralgia" Medications Work!

- ~1995 primarily amitriptyline
- ~1998 added gabapentin
- 2009, Amitriptyline, Gabapentin, Desipramine, Pregabalin, Citalopram, Effexor, Topamax Oxcarbazepine

2004 series:

- News story with viewership of 300,000 aimed at public, primary care
- ~200 patient visits to BVI in response in ~4 months
- Looked at first 112 patients to RWB
- Therefore, a self-selected population seen over ~ 3 ½ months' time, <u>n = 110</u>

Demographics

- 110 patients, self-identified with great accuracy. I.E., virtually all had SNC
- M:F is 26:84, or 76% F and 24% M
- Age range: 13-83; Mean = 58 y.o.

Duration of Coughing Syndrome

- Mean 12.7 Years
- Median 10 years
- Range: few weeks to 62 years

Mostly continuous, a few "cyclical"

Patient belief or memory about Onset / Cause

- Approximately 30% some sort of URI, including sinusitis, laryngitis, even "throat shingles."
- Approx. 20 % bronchitis
- Approximately 50 % out of the blue or *assumed* URI (no specific memory)

Duration of attack

- Major attack: 1-5 minutes (1 ½)
- Lesser attack: 5 – 30 seconds (5)

Number of Episodes per Day

- Major attack: median = 3
- Lesser attack: median = 10 (mean 30)
- During sleep: major: mean =1; Lesser attack mean = 2.26

Median is 13 spells daytime and ~3 per night

Patient Rating of Severity of the Problem

1 2 3 4 5 **6** 7

Sensation Characteristics

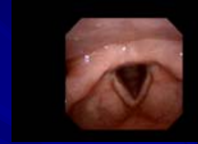
- Top three descriptions of the sensation that precedes the cough:
  - Tickle
  - Sudden dry patch— "intense sandpaper"
  - "Crumb in throat"
- Location:
  - Over half @ sternal notch
  - Most of remainder @ level of larynx
  - Mostly midline

Commonest "Triggers"

- Voice use (talking, laughing, singing)
- Eating
- Cold / warm air inhalation
- Posture change
- Smoke, strong odors
- Touching a spot on neck
- Example of Trigger Phenom.

Audio / Video Clips

- 4. Trigger with high F_o



- 5. Trigger with touching neck

Physical Responses Besides Coughing

- Nose runs
- Eyes tear
- Almost (or do) throw up
- Urinary incontinence
- Turn red
- Laryngospasm

Also: sneezing, broken ribs, ecchymosis, passed out

Continuous vs. Cyclical

- Mostly unremitting
- 10% may have long periods relatively free of symptoms or are "cyclical"
- May "crescendo" for months after URI (25%)

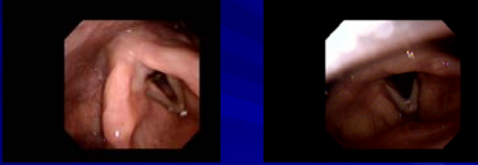
Laryngospasm . . .

Occurs in about 30% of patients at some time in course of SNC (often at onset) but in only a few is it severe or primary

Physical Examination . . .

- 10% GERD findings (but had failed PPI, etc.)
- 5% with mucosal lesion
- 50% with subtle-to-obvious neurological finding . . . Are the following over-interpreted?

Audio / Video Neurogenic Findings



Other details . . .

- Doctors seen: median 4
- Major tests done: median 4
- Medications tried: median 4
- Half of patients found something that provided partial temporary relief—especially steroids and tussionex
- 1/3 tried alternative medicine with NR

Any patterns in PMH, ACE use, smoking, surgery, etc.?

NO

Treatment: General Comments

- Patient unfamiliarity a hindrance—consider instructional video
- May require considerable tweaking of medication—labor intensive (VM)
- Don't necessarily expect "cure" but major reduction possible
- Drift downward of benefit from initial level may only mean increased dose needed (not necessarily placebo effect)

Treatment: Medical Options

- Amitriptyline (Elavil)
- Gabapentin (Neurontin)
- Desipramine for older patients
- Pregabalin (Lyrica)
- Citalopram
- Effexor, Topamax
- Oxcarbazepine (Trileptal)

- Again, may require tweaking

Amitriptyline & Desipramine

- 10-100 mg 2 h before bed
- Sometimes, divided doses
- SE: "grogginess" or dry mouth, wt. gain
- Put dose titration in pt. hands
- Aim for 85% reduction of sxs
- Expect 30-50 % NR;
- If can't achieve 85% reduction, consider moving to gabapentin

Gabapentin (Neurontin)

- Build to 300 TID (900 mg)
- Gradually increase to as much as 2700 mg per day to desired benefit or tolerance
- SE: Sleepy, "drunk," short-term memory loss, pedal edema, flashing lights
- Again, common to get 85% reduction
- Stronger benefit for some than A; others find A works better

Pregabalin (Lyrica)

- 50 mg TID building to 300 TID
- Think of 50mg of L ~= 300 mg of G
- SE like gapapentin

Citalopram

- 20 mg a day for a week
- Then, 40 mg a day
- Then, even 60 mg a day

Oxcarbazepine (Trileptal)

- Build to 600 BID
- Perhaps increase to 1200 BID
- SE: Sleepy, tired
- Monitor LFT's
- Result similar to G (very small n)

This is backup; A and G are primary medicines

Results of Treatment

- 12 patients 1999: "40-100% reduction of symptoms on 10 mg of amitriptyline
- 2 had an early decline in response
- One had inadequate benefit -> gabapentin
- 112 more recent patients: ~50% reduction on 10-30 of A (rg. 0-100%); ~50% reduction on up to 1500 G (rg 0-100%)

Selected Patient Comments: Best group

- "I didn't have to get up and leave during church—first time in 20 years, and slept through the night for the first time too"
- "Thrilled! Can take a deep breath again!"
- "Coworkers overwhelmed by change"
- "Amazing"
- "You've given me my life back"
- "I want to break out the champagne"

Selected Patient Comments (Intermediate group)

- "Much improved, but still some hard coughs."
- "70% reduction at night, only 30% during the day."
- "I still cough, but no laryngospasms"
- "Helps a lot, but __________ side effect."

Illustrates potential need for phone f/u; tweaking

Selected Patient Comments (Non-responders <10 %)

- "No response"
- "No response and I'm sleepy or ____________ from the medicine"
- "Some benefit, but SE intolerable"

Results of Treatment: a word about appropriate skepticism

- These patients had mean of 10 years' coughing, 4 doctors, 4 major treatments considerable opportunity to experience "placebo effect," but hadn't previously
- Placebo effect often transient; we've had durable responses 12 or 15 years

Summary of the DX and RX of SNC

- Characteristic history NOT that of asthma, GERD or psychogenic
- Example: Trigger phenomenon
- Neg W/U; NR to prior treatments
- Amitriptyline 10-100 mg
- IF NR or inadequate, → Gabapentin 600-1800 mg per day, with pregabalin or others in reserve

QUESTION: Primary DX--or DX of exclusion after asthma, GERD, etc.?

Summary of NC

- Consider NC as a primary diagnosis . . .
- If skeptical, perhaps try it and see what you think . . .
- Educate local primary care doctors