TRIGEMINAL NEURALGIA

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Demography

- Incidence: 4-5/100,000
- Also known as Fothergill’s disease/Tic Douloureux
- Female predominance (m: f = 1:2 ~ 2:3)
- Mean age: 50 yrs.
Why old age?

• Probably, with age
  the arteries elongate and become ecstatic
  brain sags more within the skull
Characteristics of pain

- Paroxysms of severe, lancinating, electric shock-like bouts of pain restricted to the distribution of the trigeminal nerve
  - Unilaterally (right side)
  - The mandibular (V3) and/or maxillary (V2) branch or, rarely the ophthalmic (V1) branch
- Spontaneous attack or triggered by trigger zones
- Seconds to minutes
Pain distribution
• Triggers may be shaving, brushing teeth, drinking, eating or even slight breeze
Progression of Trigeminal Neuralgia Over Time

Early in Disease Course
- Periods of Exacerbation
- Periods of Remission

Later in Disease Course
Diagnostic criteria for classic trigeminal neuralgia (IHS)

• Paroxysmal attacks of pain lasting from a fraction of a second to two minutes that affect one or more divisions of the trigeminal nerve

• Pain has at least one of the following characteristics
  – intense, sharp, superficial, or stabbing
  – precipitated from trigger areas or by trigger factors

• Attacks are similar in individual patients

• No neurological deficit is clinically evident

• Not attributed to another disorder
Types of TN

• Classic (typical TN)

• Atypical TN

• Pre-TN

• Post traumatic TN (neuropathy)

• Failed TN
Differential diagnosis

• Glossopharyngeal neuralgia
• Post herpetic neuralgia
• Sluder’s sphenopalatine neuralgia
• Geniculate neuralgia
• TM joint pain
• Cluster headache
• Dental, orbital pain or sinusitis
Etiology

- Idiopathic (vascular)
- Tumors (V nerve schwannoma, CPA tumors)
- Human herpes simplex virus
- Multiple Sclerosis
  - 4% patients with MS have TN
  - 2% patients with TN have MS
Vascular

- Aberrant loop of artery or vein found to be compressing the root entry zone of the Vth nerve in 80-90% of patients at surgery

- The nerve is demyelinated next to the compressing vessel

- Eliminating the compression provides long term relief

- Compression by tumours or the demyelinating plaques of multiple sclerosis produce similar lesions of the root entry zone
### Vascular compression (Janetta et al 1996)

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Total(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCA</td>
<td>909(75.5%)</td>
</tr>
<tr>
<td>AICA</td>
<td>116(9.6%)</td>
</tr>
<tr>
<td>PICA</td>
<td>8(0.7%)</td>
</tr>
<tr>
<td>VA</td>
<td>19(1.65)</td>
</tr>
<tr>
<td>BA</td>
<td>9(0.7%)</td>
</tr>
<tr>
<td>LA</td>
<td>3(0.2%)</td>
</tr>
<tr>
<td>Unnamed artery</td>
<td>186(15.4%)</td>
</tr>
<tr>
<td>Vein</td>
<td>822(68.2%)</td>
</tr>
<tr>
<td>Vein and artery</td>
<td>671(55.7%)</td>
</tr>
<tr>
<td>Vein only</td>
<td>151(12.5%)</td>
</tr>
</tbody>
</table>
Why is trigeminal neuralgia paroxysmal?

• Compression of the REZ leads to demyelination and axonal damage

• Damaged axons become electrically hyperexcitable, exude neurotransmitters and potassium into the interstitial space, and crucially can repetitively fire at high frequency

• Demyelination leaves bare axons, often subserving different sensory modalities such as light touch and pain in contact with one another; this allows ephaptic transmission directly between them
Why is trigeminal neuralgia paroxysmal?

- A "spark"—often from light touch or cold in a trigger zone—"ignites" a self fuelling "inferno" of electrical discharge dependent upon all the above mechanisms. This rapidly burns itself out as axons become hyperpolarized, leading to the sudden and merciful cessation in pain and characteristic refractory period of a minute or so during which further pain cannot be triggered.
Investigations

• Whether there is an identifiable cause of the disease, particularly with a view to surgical cure
• Scan should be obtained in
  1. younger patients
  2. atypical clinical features, including sensory loss or a dull burning pain between paroxysms
  3. patients who do not respond to initial medical therapy.
• 3D CISS with MPR sequences and MRA
• 90.5% sensitivity and 100% specificity
Management

• Medical treatment
  – Carbamazepine (Tegretol) – first line
  – Oxcarbazepine
  – Gabapentin (Neurontin)
  – Lamotrigine
  – Baclofen
  – Phenytoin
  – Clonazepam
  – Valproate
  – Mexiletine
  – Topiramate
Carbamazepine (mazetol/tegretol)

- 1\textsuperscript{st} line treatment (1961)
- Sodium-channel modulator - Antiepileptic drug
- Initial response is virtually universal
- By 10 yr it drops to 50%
- Lack of response ??? diagnosis
- Start at 100 mg bid (200 mg/d)
  Add up to 200 mg/d in increments of 100 mg every 12 hr.
- Maximum dose 1200 mg/day.
Carbamazepine (mazetol/tegretol)

Side effects

- Dermatological: rash, Steven Johnson, EM
- Idiosyncratic (2-6%): Aplastic anemia
- Somnolence/dizziness/nausea/nystagmus/hepatic dysfunction/hyponatremia
- Drug interactions
Carbamazepine (mazetol/tegretol)

**Monitoring treatment**

- CBC/LFT/RFT prior to start of treatment
- Every 2 weeks for 2 months
- Every 3 monthly thereafter
- Stop if TLC<3000/microl
Oxcarbamazepine (oxetal)

- Pain relief similar to carbamazepine but fewer side effects or drug interactions
- Sodium-channel modulator, calcium-channel modulator.
- 300 mg bid. Maximum 2400 mg/day when given as monotherapy
- Dizziness, diplopia, ataxia, nausea, somnolence, headache, hyponatremia (more often than with carbamazepine)
- 300 mg of oxcarbazepine is equivalent to 200 mg of carbamazepine
Baclofen

• Some people advocate it as 1st line
• 5-10 mg tid. Increase by 10 mg every other day until 60-80 mg daily
• Few drug interactions
• Ataxia, lethargy, GI intolerance
• Possibly synergistic with phenytoin/carbamazepine
• Benefit shown on randomized controlled trials
Phenytoin (Dilantin/eptoin)

- Antiepileptic drug, sodium-channel modulator
- 100 mg po tid, or 300 mg once per day
- Comes in an intravenous form for acute exacerbation of pain
- Many drug interactions; Ataxia, slurred speech, rash
- Monitor blood levels
- Response rate 25-60%
Surgical treatment

– *Gasserian ganglion-level procedures*
  • Microvascular decompression (MVD)
  • Ablative treatments
    – Radiofrequency thermocoagulation (RFT)
    – Glycerol rhizolysis (GR)
    – Balloon compression (BC)
    – Stereotactic radiosurgery (SRS)

– *Peripheral procedures*
  • Peripheral neurectomy
  • Cryotherapy (cryoanalggesia)
  • Alcohol block
Radiofrequency thermocoagulation

• 1st explored by Kirchner, modified to produce more precise and safer lesions by Sweet (1974)
• Selective partial lesioning of the affected ganglion or retrogasserian root
• Intermittently anaesthetized patient under fluoroscopic control
• Needle is inserted through the foramen ovale into Meckel’s cave using bony landmarks
• Once the needle has travelled the pre-planned distance, the patient is allowed to awake, the stylet replaced by the electrode and stimulation of the nerve root carried out.
Radiofrequency thermocoagulation

• Once appropriate siting has taken place, the patient is anaesthetized again for thermal lesioning
• This is performed in cycles of 45 to 90 s at temperatures of 60–90°C
• After each lesioning the patient is awakened and manual sensory testing of the face carried out
• Additional thermal lesions performed until clear hypalgesia has ensued
complications

• dysesthesias (20%),
• masticatory muscle weakness (23%)
• absent corneal reflex (6%)
• keratitis (2%),
• anesthesia dolorosa (1%)
• meningitis (0.2%).
Glycerol rhizolysis

• discovered serendipitably
• Leksell and Häkanson injected tantalum dust mixed with glycerol into the trigeminal cistern as a marker for radiosurgery
• patient cooperation is not necessary
• localization of the target is performed using intraoperative cisternography
• lower risk of facial sensory loss compared with either RFT or BC
Test dose: 0.1-0.15 ml
0.05~0.1 ml at 3~5 min. intervals
Total dose: 0.1~0.4 ml
(average volume of the trigeminal cistern is 0.25 ml, and rarely >0.4ml)

Sensory changes: pain, burning or paresthesia
Initial pain relief >80%, recurrences 10-50% at 1 yr
Balloon compression

• Pear-shape balloon
• Compression time: 1~7 min.
• compresses the retrogasserian fibers against the firm edge of the dura and petrous ridge
Immediate pain relief in almost all, 6–14% recurrence in the first year

dysesthesias and masseter weakness can occur
Peripheral procedures

- Peripheral neurectomy
- Alcohol block 0.15-1.5 ml of 80-100% alcohol
- Whole branch and small peripheral branches
- Cryotherapy
  - Exposed surgically and direct application of cryoprobe -50 to -140 celsius
  - 3 cycles of 2 min with a 5 min thaw in between
Ganglion-level procedures vs. Peripheral procedures

- Ganglion-level ablative procedures
  - Similar long-term success rate
  - Varying degrees of sensory loss
  - Balloon compression least likely to impair corneal sensation or to cause anesthesia dolorosa

- Peripheral procedures
  - High recurrence rates
  - No benefit over ganglion-level procedures
  - Reserved for emergency use
Microvascular decompression (MVD)

- Concept of Dandy (1920)
- Popularized by Janetta
- Gold standard as it deals the underlying cause
- Suboccipital craniotomy, retraction of superolateral margin of cerebellum arachnoid is dissected and vessel freed, piece of shredded teflon felt placed between the vessel and the nerve to separate them.
- Veins, if any, coagulated and divided
Microvascular decompression (MVD)

• Of 1185 patients treated by Barker et al with mean follow up of 6.5 years, 70% had excellent results at 10 yrs

• Most recurrences within 1\(^{st}\) two years.
Recurrence???

- Female sex
- Symptoms lasting >8 years
- Venous compression of the trigeminal root entry zone
- Lack of immediate postoperative cessation of pain
- Repeat posterior fossa exploration can be attempted
Stereotactic radiosurgery

• Pioneered by Lars Leksell (1953)
• An ablative procedure
• **Target**- Gassserian Ganglion, Far anterior Target & REZ
• LINAC/GK/Cyberknife
• In GK, dose used is 70-90 Gy
• Mean time to pain relief is approximately one month
• Focal axonal degeneration and necrosis
## Outcome of GK Radiosurgery

<table>
<thead>
<tr>
<th>Author (yr)</th>
<th>No. of pt.</th>
<th>max.dose(Gy)</th>
<th>Median f/u (m)</th>
<th>Pain free(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kondziolka, '98</td>
<td>106</td>
<td>70-90</td>
<td>18m</td>
<td>60%</td>
</tr>
<tr>
<td>Nicol,2000</td>
<td>42</td>
<td>90</td>
<td>14m</td>
<td>74%</td>
</tr>
<tr>
<td>Maesawa,2001</td>
<td>220</td>
<td>60-90</td>
<td>22m</td>
<td>55%</td>
</tr>
<tr>
<td>Pollock,2002</td>
<td>117</td>
<td>70-90</td>
<td>26m</td>
<td>75%</td>
</tr>
<tr>
<td>Brisman,2004</td>
<td>293</td>
<td>75-77</td>
<td>23m</td>
<td>51%</td>
</tr>
<tr>
<td>Regis, 2006</td>
<td>100</td>
<td>70-90</td>
<td>NA</td>
<td>82%</td>
</tr>
<tr>
<td>Longhi,2007</td>
<td>160</td>
<td>85</td>
<td>36m</td>
<td>61%</td>
</tr>
</tbody>
</table>
Positive predictors

• Absence of MS

• Higher dose

• Primary radiosurgery

• Proximity of isocentre to brainstem
## Primary vs. secondary GK

<table>
<thead>
<tr>
<th>Study</th>
<th>Pt.</th>
<th>1 yr(%)</th>
<th>2yr(%)</th>
<th>3yr(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pollock 2002</td>
<td>117</td>
<td>67</td>
<td>67</td>
<td>67</td>
</tr>
<tr>
<td>primary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>secondary</td>
<td></td>
<td>51</td>
<td></td>
<td>46</td>
</tr>
<tr>
<td>Fountas, 2006</td>
<td>77</td>
<td>81</td>
<td>69</td>
<td>54</td>
</tr>
<tr>
<td>primary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>secondary</td>
<td></td>
<td>64</td>
<td>44</td>
<td>12</td>
</tr>
</tbody>
</table>
Complications

- Facial dysesthesias
- Anesthesia dolorosa (disabling painful facial numbness)
- Isolated reports of dysguesia, facial weakness, dry eye etc
## AllMS experience

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of patients</strong></td>
<td>17</td>
</tr>
<tr>
<td>Male: female</td>
<td>10:7</td>
</tr>
<tr>
<td>Right: left</td>
<td>11:6</td>
</tr>
<tr>
<td>Age</td>
<td>32-78yr (mean 56yr)</td>
</tr>
<tr>
<td>Mean follow up</td>
<td>15months(3-48months)</td>
</tr>
<tr>
<td>Primary/secondary/repeat</td>
<td>6/11/1</td>
</tr>
<tr>
<td>Mean pain duration</td>
<td>9.85 yrs (1-25 yr)</td>
</tr>
</tbody>
</table>
Radiosurgical procedure

- Single isocentre, median dose of 80 Gy (80–90 Gy) to the 100% isodose line using a 4 mm collimator

- Target: REZ

- No part of the brainstem received dose of > 12 Gy
Results

- Poor
- Fair
- Good

No of patients: 5/8

Outcome categories based on patient results:
- Excellent
- Good
- Fair
- Poor

TRIGEMINAL NEURALGIA  AIIMS
Analysis of results

• None of our patients had excellent result

• 70-80% overall relief in various series

• Why we failed?
  • low dose/more secondary procedures
  • prolonged duration of symptoms/inadequate MR sequences
  • shorter Vth nerve in asians / resistance to radiation
THANKS FOR ATTENTION