3. Cluster headache and other trigeminal autonomic cephalalgias

- 3.1 Cluster headache
  - 3.1.1 Episodic cluster headache
  - 3.1.2 Chronic cluster headache
- 3.2 Paroxysmal hemicrania
  - 3.2.1 Episodic paroxysmal hemicrania
  - 3.2.2 Chronic paroxysmal hemicrania (CPH)
- 3.3 Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)
- 3.4 Probable trigeminal autonomic cephalalgia
  - 3.4.1 Probable cluster headache
  - 3.4.2 Probable paroxysmal hemicrania
  - 3.4.3 Probable SUNCT

* Coded elsewhere: 4.7 Hemicrania continua, whose cranial autonomic features are less constant, is to be found under 4. Other primary headaches.
Paroxysmal hemicrania - epidemiology

- The prevalence is very low, exact figures are not known.
- It is estimated that the paroxysmal hemicranias comprise about 3-6% of all TAC.
- The headaches usually start between the age of 20 and 40 years.
- Male to female ratio is 1:3

3.2 Paroxysmal hemicrania

- Description:
- Attacks with similar characteristics of pain and associated symptoms and signs to those of cluster headache (Attacks of severe, strictly unilateral pain which is orbital, supraorbital, temporal or in any combination of these sites, associated with one or more of the following, all of which are ipsilateral: conjunctival injection, lacrimation, nasal congestion, rhinorrhea, forehead and facial sweating, miosis, ptosis, eyelid oedema )
- but they are shorter-lasting, more frequent, occur more commonly in females and respond absolutely to indomethacin.
3.2 Paroxysmal hemicrania

- Diagnostic criteria:
  - A. At least 20 attacks fulfilling criteria B–D
  - B. Attacks of severe unilateral orbital, supraorbital or temporal pain lasting 2–30 minutes
  - C. Headache is accompanied by at least one of the following:
    1. ipsilateral conjunctival injection and/or lacrimation
    2. ipsilateral nasal congestion and/or rhinorrhea
    3. ipsilateral eyelid oedema
    4. ipsilateral forehead and facial sweating
    5. ipsilateral miosis and/or ptosis
  - D. Attacks have a frequency above 5 per day for more than half of the time, although periods with lower frequency may occur
  - E. Attacks are prevented completely by therapeutic doses of indomethacin
  - F. Not attributed to another disorder

Paroxysmal hemicrania – treatment

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Attack treatment</td>
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</tr>
<tr>
<td>Prophylactic treatment</td>
<td>Indomethacin (A)</td>
</tr>
<tr>
<td></td>
<td>Verapamil (C)</td>
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<tr>
<td></td>
<td>NSAIDs (C)</td>
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<td>Topiramate (C)</td>
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A – effective, B – probably effective, C – possibly effective
By definition, indomethacin in a daily dose of up to 200mg is completely effective. Indomethacin should be administered in three or more doses per day because of its short half-life time of 4 h. Many patients need high dose of indomethacin only in the first weeks of treatment, than a lower dose can be tried. The major contraindication is gastrointestinal disorder. The major side effects are gastrointestinal discomfort and bleedings. Therefore, a proton pump inhibitor should be given in addition. For diagnostic and rapid therapeutic purposes, the so-called indo-test has been suggested. Intramuscular indomethacin 50 mg should result in freedom of attacks within 30 min.

Case No 1

♂, 45
Two types of headache

The first type of headache:
Onset at the age of 25
Occurring in periods
3 attacks per day, lasting for 75 minutes
unilateral, left-sided
accompanied by ipsilateral ptosis, lacrimation and rhinorrhoea
effective therapy: oxygen (inh.), sumatriptan (inj.)
Case No 1

- Diagnosis?
- Cluster headache
- Paroxysmal hemicrania
- SUNCT

Case No 1

- The second type of headache:
  - 15 attacks per day, lasting for 15 minutes
  - unilateral, left-sided
  - accompanied by ipsilateral ptosis, lacrimation and rhinorrhea

- inefficient therapy: oxygen (inh.), sumatriptan (inj.)
- effective prophylactic treatment: indomethacin 150 mg daily orally
Case № 1

• Diagnosis?
  • Cluster headache
  • Paroxysmal hemicrania
  • SUNCT

Case № 1
Cluster headache and paroxysmal hemicrania

• Some patients have been described who have two types of trigeminal autonomic cephalalgias.
• They should receive both diagnoses.
• Both conditions must be treated for the patient to be headache free.

• Differentiation is based on:
  • Duration and frequency of attacks
  • Efficiency of the indomethacin therapy
3.3 Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)

- **Description:**
  - This syndrome is characterised by short-lasting attacks of unilateral pain that are much briefer than those seen in any other TAC and very often accompanied by prominent lacrimation and redness of the ipsilateral eye.

- **Diagnostic criteria:**
  - **A.** At least 20 attacks fulfilling criteria B–D
  - **B.** Attacks of unilateral orbital, supraorbital or temporal stabbing or pulsating pain lasting 5–240 seconds
  - **C.** Pain is accompanied by ipsilateral conjunctival injection and lacrimation
  - **D.** Attacks occur with a frequency from 3 to 200 per day
  - **E.** Not attributed to another disorder
SUNCT - epidemiology

- incidence - 1.2/100,000
- prevalence - 6.6/100,000, Williams and Broadley 2008
- a rare syndrome
- Case series (52 cases), Cohen et al. 2006
- Case series (24 cases), Williams and Broadley 2008
- has male predominance, with sex ratio 1.3 : 1
- the typical age of onset is between 35 and 65 years (68% of primary SUNCT cases), but ranges from 10 to 77 years

SUNCT - site of pain

- the pain usually is maximal in the ophthalmic distribution of the trigeminal nerve, especially the orbital or periorbital regions, forehead, and temple
- it may radiate to the other ipsilateral trigeminal divisions and, rarely, even to extratrigeminal regions such as the
  - ear and Pareja JA and Sjaastad O 1997, Graff-Radford SB 2000
  - the occiput D’Andrea G et al. 2001
- There is one case report of extratrigeminal SUNCT syndrome with pain centered on the throat without trigeminal involvement
  Wingerchuk DM et al. 2000
SUNCT - laterality of attack

• Attacks typically are strictly unilateral and side-locked (88%)
• The pain is present more frequently on the right side (60%)

• But, there are reports of:
  • strictly unilateral, but side-alternating attacks D’Andrea G and Granella F 2001

SUNCT - severity of pain

• Intensity of pain is between severe and excruciating in most of the patients and ...

• moderate in only a small number of patients.
SUNCT - character of pain

- The pain has a neuralgic character in most of the patients, usually being described as stabbing, sharp, burning, pricking, piercing, shooting, lancinating, or electric shock-like.

- Otherwise, it can be pulsatile, throbbing, steady, spasmodic or staccato.

SUNCT - duration of the individual attack

- **between 5 and 240 seconds** – ICHD-II, diagnostic criterion

- But, there are reports of lasting:
  - **between 2 and 600 seconds**  *Black DF and Dodick DW, 2002*
  - **between 8 and 20 minutes**  *Matharu et al. 2003*
  - **between 1 and 2 hours**  *Pareja JA et al. 1996, May A et al. 1999, Matharu MS et al. 2002*

- Most patients are completely **pain-free between attacks**, although there are reports of a dull interictal ipsilateral **discomfort** over the same site, continuous and intermittent.

- In addition, a **burning sensation** lasting 2 hours after the attacks has been reported.
SUNCT - frequency and periodicity of attacks

• In most patients, SUNCT syndrome occurs in an episodic manner, the temporal pattern is variable, with the symptomatic periods alternating with remissions in an erratic manner.

• Symptomatic periods generally last from a few days to several months and occur once or twice annually, although a maximum of 22 episodes per year have been reported Pareja JA et al. 1997.

• Remissions typically last for a few months, but can last from 1 week to 8.5 years Jimenez-Huete A et al. 2002

• Symptomatic periods appear to increase in frequency and duration over time.
• Circannual periodicity is NOT a typical feature of SUNCT.

SUNCT - frequency and periodicity of attacks

• There are case reports in which the disorder is chronic, with the symptomatic period lasting for more than 1 year.

• In some reported cases:
  • episodic at onset before transforming into the chronic form Lain AH et al. 2000, Leone M et al. 2000.
  • chronic phase alternated with the episodic phase Hannerz J et al. 2002.

• The chronic form of SUNCT now is sufficiently validated?
• The subclassification of SUNCT syndrome should include both, episodic and chronic forms?
SUNCT - frequency and periodicity of attacks

• The attack frequency during the symptomatic phase varies among sufferers and within an individual sufferer.

• Attacks may be as infrequent as once daily or less to more than 200 per day.

• There are case reports of a SUNCT-like status, which is when patients experience severe exacerbations with frequent, easily triggered, high-intensity pain attacks in a repetitive and overlapping fashion for several hours or days at a time Montes E et al. 2001.

SUNCT - frequency and periodicity of attacks

• SUNCT attacks occur exclusively or predominantly during the daytime.

• Nocturnal attacks were reported to occur occasionally
**SUNCT - associated features**

- “always” present and very prominent:
  - ipsilateral conjunctival injection (100%) and lacrimation (94%) - usually begin 1 to 2 seconds after the onset of the pain and may outlast the pain by a few seconds
- reported less commonly:
  - ipsilateral rhinorrhea (54%), nasal congestion (48%), eyelid edema (26%), ptosis (12%), miosis (4%), and facial sweating (8%) or redness (2%)

  *Matharu et al. Cephalalgia 2003*

- NOT associated with SUNCT syndrome normally:
  - restlessness
  - nausea (2%), vomiting, photophobia (4%), phonophobia, osmophobia
  - aura

**SUNCT - triggers**

- Most patients with SUNCT syndrome have **spontaneous and triggered attacks.**
- Most patients can precipitate attacks by touching certain trigger zones within trigeminal innervated distribution and, occasionally, even from an extratrigeminal territory. Precipitants include touching the face or scalp, washing, shaving, eating, chewing, brushing teeth, talking...

- Some patients seem to exhibit **exclusively spontaneous attacks.**

- None of the patients had exclusively triggered attacks.
SUNCT - refractory period

- Most patients with SUNCT have no refractory period.
- There has been only one case report of absolute refractory periods in SUNCT syndrome.  
  \[\text{Matharu et al. 2002}\]
- However, most case reports of SUNCT syndrome make no mention of a refractory period. This may be because of a lack of awareness of this feature; consequently, the lack of a refractory period in SUNCT syndrome may be under-reported.

SUNCT – physical examination

- The physical examination is normal in most patients with SUNCT syndrome.
- Slight allodynia or hyperesthesia over the ophthalmic and mandibular trigeminal divisions has been reported.  
  \[\text{Graff-Radford SB et al. 2000}\]
- Ophthalmic division hypoesthesia and corneal hyperesthesia have been reported too.
- Horner’s syndrome is not a feature of SUNCT.
SUNCT - differential diagnosis

- The differential diagnosis of very brief headaches includes:
  - SUNCT (primary and secondary forms)
  - trigeminal neuralgia
  - primary stabbing headache
  - paroxysmal hemicrania

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<tr>
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</tr>
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<td>sporadic</td>
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</tr>
<tr>
<td>Indomethacin - responsive</td>
<td>yes</td>
<td>no</td>
<td>yes/no</td>
<td>no</td>
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</table>
SUNCT - treatment

• There is no consistently effective treatment known for SUNCT syndrome.
• No controlled trials have been published, and the rareness of the syndrome makes this a difficult task.
• However, some case reports have been published with individual efficacy of some drugs.
• Because of the extreme burden caused by this disorder, all reasonable treatment options should be tried.
• Among all drugs tried in SUNCT syndrome, lamotrigine was most efficacious in the published case reports.

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<td>lamotrigine (C)</td>
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A – effective, B – probably effective, C – possibly effective


SUNCT - treatment

OTHER TREATMENT OPTIONS

<table>
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<tr>
<th>Drug</th>
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<tbody>
<tr>
<td>topiramate</td>
<td>Rossi P et al. 2003, Kuhn J et al. 2005</td>
</tr>
<tr>
<td>oxcarbazepine</td>
<td>Dora B et al. 2006</td>
</tr>
<tr>
<td>verapamil</td>
<td>Narbone MC et al. 2005</td>
</tr>
<tr>
<td>intravenous lidocaine</td>
<td>Matharu MS et al. 2004</td>
</tr>
<tr>
<td>steroids</td>
<td>De Lourdes Figuerola M et al. 2009</td>
</tr>
<tr>
<td>intravenous phenytoin</td>
<td>Schwaag S et al. 2003</td>
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</table>

• In summary, no recommendation can be given for the treatment of SUNCT syndrome.
• Treatment with lamotrigine (at least 100 mg) is considered the first-line option.
Case № 2

- A 24-year-old, right-handed female
- 6-year history of headaches

- Previous medical history was unremarkable.
- There is no family history of headaches.
- She is non-smoker and never drinks alcohol.
- She has regular menstrual cycles, denies galactorrhoea or problems in her sexual intercourse.
- She is the student of economics, with low success rate for which she blames her headaches.


Case № 2

- Headache onset: at age of 18
- There were no precipitants at onset.
- A typical attack was bilateral with pain affecting both sides simultaneously.
- The pain was centered on the retro-orbital region and temple with radiation to the occipital regions.
- The pain had an electric shock-like quality and came on rapidly, was maintained at plateau phase and then resolved rapidly.

- According to pain severity, duration and frequency, she distinguished two types of attacks.
Case No 2

- The first type of attack:
  - occurred every 15 to 20 minutes
  - moderate in intensity (6 / 0 – 10)
  - lasted for 5 to 6 seconds and
  - was associated with feeling of clouded vision

Case No 2

- The second type of attack:
  - occurred several times a day in no predictable fashion, never less than 5 and never more than 10 daily
  - severe in intensity (9 / 0 – 10)
  - lasted for 30 seconds and
  - was associated with prominent conjunctival injection, lacrimation and periorbital face flushing
Case No 2

• She had attacks only when awake and was completely pain free during sleep
• She denied photophobia, phonophobia, osmophobia, nausea or vomiting as well any aura symptoms.
• There was no background pain.
• She felt drowsiness during both types of attacks.
• Head movements, talking, eating, and blowing nose or other manipulations could not trigger the attacks.
• During the first two years of her headaches she had only the first type of attacks with moderate pain. At the further course she had daily attacks of both types without any remission periods.
• There was no seasonal variation of attacks’ severity or frequency.

Case No 2

• Unsuccessful treatment attempts:
  • Aspirin
  • Diclofenac
  • Paracetamol/caffeine combinations
  • Amitriptyline 75 mg daily
  • Sodium valproate 1000 mg daily

• At the time of presentation she was taking carbamazepine 800 mg daily, which had reduced the frequency of milder attacks for about 30% and had no effect on attacks of higher intensity.
Case № 2

• physical and neurological examination were normal

• Observed attacks:
  • 4 attacks of moderate intensity lasting 7, 7, 9 and 10 seconds, as well as
  • 2 attacks of severe pain intensity lasting 35 and 47 seconds

• The conjunctival injection, lacrimation and face flushing were more prominent during more severe attacks.

• In spite of patient’s statement that pain is simultaneous and had equal intensity on both sides, we observed that the autonomic features were more prominent on the right.

Case № 2

• Examinations with normal results:

• Routine hematological and biochemical screening

• Electroencephalography, after serial and sleep-deprivation monitoring

• Blink reflex

• MRI scan of the brain

• MR angiography
Case № 2

• A trial of high-dose oxygen inhalation at flow rate 15 l/min and

• subcutaneous sumatriptan 6 mg had no effect.

• Indomethacin administered in three doses of 25 mg per day was ineffective, as well as further dose increment that stopped at daily dose of 125 mg because of constant dull headache.

Case № 2

• Diagnosis?

• Cluster headache

• Paroxysmal hemicrania

• Probable SUNCT
very brief headaches - differential diagnosis

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Case № 2 - 3.4.3 Probable SUNCT

- Diagnostic criteria:
  - A. Attacks fulfilling all but one of criteria A–D for 3.3 SUNCT
    - A. At least 20 attacks fulfilling criteria B–D
    - B. Attacks of unilateral orbital, supraorbital or temporal stabbing or pulsating pain lasting 5–240 seconds
    - C. Pain is accompanied by ipsilateral conjunctival injection and lacrimation
    - D. Attacks occur with a frequency from 3 to 200 per day
  - B. Not attributed to another disorder
Bilateral Trigeminal Autonomic Cephalgias

- **Cluster headache**, Sjøastad O et al. 1985; Durko A. and Bogucki A. 1984
- In our group consisted of 160 patients with cluster headache:
  - 1 patient had bilateral attacks and
  - 2 patients had side-switching attacks


Case No 2

- **Gabapentin**, given at daily dose of 1200 mg, was ineffective.

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</table>

- **Lamotrigine 150 mg** per day - set the patient free of any severe attacks and had diminished frequency of moderate intensity attacks.
- **Lamotrigine 200 mg** per day completely suppressed attacks during first month.
- During one-year follow-up she had periods of 3 months without attacks, shifting with periods of the same duration with no more than 10 mild attacks daily.
- In this period she successfully completed her year’s examinations.
Case No 2


<table>
<thead>
<tr>
<th>84 patients with pituitary tumor and headache</th>
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<tbody>
<tr>
<td>Migraine</td>
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<tr>
<td>SUNCT</td>
</tr>
<tr>
<td>Cluster Headache</td>
</tr>
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</tr>
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</tr>
<tr>
<td>Headache - unclassified</td>
</tr>
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</table>

- and despite the fact that there were no symptoms and signs of hormonal disturbances, we performed MRI scan of pituitary-hypothalamic region and examination of pituitary hormones.

Case No 2

- MRI revealed the pituitary microadenoma at the right side of the gland without extending towards the surrounding structures.
Case No 2

• Serum prolactin levels were 2125 mIU/L (normal range 130-700)

• Levels of follicle stimulating hormone, luteinizing hormone, oestradiol, adrenocorticotropic hormone, basal cortisol, thyroid-stimulating hormone, free thyroxin, insulin, and growth factor were within normal range, so multiple endocrine neoplasm was ruled out.

• The treatment with bromocriptine was started.

Case No 2

• Outcome, 2 years later

• Without treatment
• Without headache
• Hormonal status – normal
• Control MRI scan of pituitary-hypothalamic region – normal
• Graduated
Paroxysmal hemicrania
and other trigeminal autonomic cephalalgias

Ana Podgorac
Belgrade, May 2012