Teaching course TC1

Rare cases in Clinical Practice: Headache

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Learning Objectives

Enable participants to:

- Identify unusual headache disorders to be considered in everyday neurological practice.
- Recognise clues to indicate that the diagnosis is an unusual one
- Identify which patients might require investigations beyond the usual routine ones.
- Respond to a diagnostic challenge and enjoy the achievement in making a correct but rare diagnosis.

Key message

- Most cases of headache that a neurologist sees will be:
  - Migraine
  - Other common primary headaches (cluster, TTH)
  - Secondary headaches which are easily diagnosed
- However many cases require consideration of:
  - Less easily diagnosed secondary headaches
  - Less common primary headaches:
    - Trigeminal autonomic cephalalgias
    - Other rare primary headaches

Cases

- A series of cases will be presented and their diagnosis and treatment will be discussed
- Conditions which may be presented are summarised in the following slides

Spontaneous Intracranial Hypotension

- Headaches developing after a lumbar puncture or epidural injection raise the possibility of low intracranial pressure, especially if aggravated by the upright posture.
- Similar headaches may develop spontaneously (for example, from leakage of cerebrospinal fluid from a nerve root sleeve).
- **MRI scan of the brain (with contrast) may show a very characteristic appearances** including dural enhancement, pituitary engorgement, subdural hygroma or haematoma and downward displacement or flattening of the brainstem.
- The headache may occur immediately or within seconds of assuming an upright position and resolve quickly (within 1 minute) after lying horizontally. But it may show delayed responses (minutes or hours) to postural change, both for worsening after of being upright and for improving (but not necessarily resolving), after lying down.
- **The orthostatic nature of the headache may become much less obvious over time.**
- Autologous epidural blood patches (EBPs) are frequently effective in sealing CSF leaks, but not always and the response to a single EBP may not be permanent
- In some cases detailed investigation to localise the leak is required and may lead to targeted blood patches or surgical intervention.
- Modern imaging to localise the leak might include CT or MRI myelography or, less often now, radionucleide cisternography

Reversible cerebral vasoconstriction syndrome: RCVS

- Reversible cerebral vasoconstriction syndrome (RCVS) may cause single or recurrent episodes of instantaneous headache.
- **RCVS and subarachnoid haemorrhage are therefore the major differential diagnoses for patients presenting with thunderclap headache.**
- CTA or MRA may show vasospasm, but this may not be apparent immediately; the radiological changes may appear a few days after the initial presentation with headache.
- Very focal sulcal subarachnoid haemorrhage may be seen in patients with this condition.
- Localised cerebral ischaemia and infarction may occur after some delay in RCVS
- Thus the tendency of emergency physicians to exclude SAH and then dismiss the patient is of concern
- RCVS may be triggered by various stimuli, often of an adrenergic nature, (such as cocaine or amphetamine use) and also by sexual activity.

Primary headache associated with sexual activity

- Two subtypes of primary headache are associated with sexual activity ('benign sex headache').
  - The less common form is pre-orgasmic and usually starts as a dull bilateral ache as sexual excitement increases. The ache is felt in the head and neck and is associated with awareness of neck and/or jaw muscle contraction.
  - The more common, and more severe, form occurs at orgasm and is explosive and instantaneous in onset. It is thus a form of 'thunderclap headache' and subarachnoid haemorrhage must be the provisional diagnosis until definitely excluded.
- The headache of orgasmic headache is severe and patients are typically appropriately anxious about a serious cause; once this is excluded, they remain anxious about the effect recurrent headaches might have on their quality of life.
- The natural history of orgasmic headache is for recurrences to occur (with sexual activity or with lifting or straining) over a period of a few weeks and then for the condition to subside.
- During the period of susceptibility, indomethacin may provide some symptomatic relief and there is some anecdotal evidence that beta blockers (such as propranolol) or calcium channel blockers (such as verapamil) may also be of value (all off label uses).
- There are many similarities between orgasmic headache and the thunderclap headache seen in reversible cerebral vasoconstriction syndrome (RCVS).It is tempting, therefore, to conclude that many cases of orgasmic headache may be a version of RCVS as suggested by Yeh et al (see next slide)

Benign sex headache & RCVS

- Taiwanese clinic based study
- 30 patients (16 M, 14 F), mean age 40, with headache associated with sexual activity None of the patients had neurological deficits at onset.
- 20 patients (67%) had secondary causes identified, including:
  - one subarachnoid hemorrhage,
  - one basilar artery dissection, and
  - **18 cases reversible cerebral vasoconstriction syndrome (RCVS).**
- Ten patients (33%) had primary HSA.
- The demographics, headache profiles, drug response and clinical course were similar between primary and secondary HSA.

Table 2. Comparisons between patients with primary HSA and RCVS

Characteristic	Primary HSA ($N = 10$)	RCVS ($N = 18$)	p value
Male (%)	5 (50%)	9 (50%)	1.000
Mean age at onset	40.2 ± 8.7	40.1 ± 10.6	0.943
Comorbidities			
Hypertension	3 (30%)	4 (22%)	0.674
Migraine	5 (50%)	4 (28%)	0.210
Tension	2 (20%)	0	0.119
HSA subtypes			0.526
Pre-orgasmic	1 (10%)	1 (6%)	
Orgasmic	7 (70%)	14 (78%)	
Post-orgasmic	1 (10%)	0	
Mixed	1 (10%)	3 (16%)	
Bilateral	8 (80%)	14 (78%)	1.000
Location			
Occipital	8 (80%)	14 (78%)	1.000
Temporal	3 (90%)	8 (44%)	0.689
Vertex	4 (40%)	5 (28%)	0.677
Whole head	2 (20%)	4 (22%)	1.000
Frontal	0	1 (6%)	1.000
Quality			
Explosive	8 (80%)	14 (78%)	1.000
Throbbing	9 (90%)	11 (61%)	0.194
Lancinating	3 (30%)	4 (22%)	0.674
Dull	4 (40%)	5 (28%)	0.667
Stabbing	4 (40%)	2 (11%)	0.147
Ripping	2 (20%)	1 (6%)	0.284
Duration			0.338
<5 minutes	1 (10%)	2 (11%)	
5–30 minutes	3 (30%)	7 (39%)	
30 minutes–4 hours	2 (20%)	7 (39%)	
4–24 hoours	4 (40%)	2 (11%)	
Frequent attacks	9 (90%)	17(94%)	1.000
Associated features			
Nausea	4 (40%)	2 (11%)	0.147
Vomiting	2 (20%)	1 (6%)	0.284
Photophobia	3 (30%)	2 (11%)	0.315
Phonophobia	4 (40%)	6 (33%)	1.000
Neck pain	5 (50%)	2 (11%)	0.063
Dizziness	6 (60%)	4 (22%)	0.097
Response to indomethacin	5/7 (71%)	9/12 (75%)	1.000
Clinical course			
Episodic	4 (40%)	13 (72%)	0.125
Relapse in episodic HSA	0/4	5/13 (39%)	0.261
Remission in chronic HSA	2/6 (33%)	1/5 (20%)	1.000

HSA, headache associated with sexual activity; RVCS, reversible vasoconstriction syndrome.

SUNCT & the TACs

Table 1: Clinical Features of the Trigeminal Autonomic Cephalgias			
	Cluster	**Paroxysmal Hemicrania**	**SUNCT**
Sex	M>F	M=F	M~F
Pain			
Type	Stabbing, boring	Throbbing, boring, stabbing	Burning, stabbing, sharp
Site	Orbit, temple	Orbit, temple	Periorbital
Frequency attacks	0.5 - 8 / day	1-40 / day (usually >5/day)	3-200 / day
Duration of attack	15-180 min	2-30 min	5-240 sec
Autonomic Features	Yes	Yes	Yes (esp. conjunctival injection & lacrimation)
Migrainous Features	Yes	Yes	Yes, in ~ 1/3
Alcohol trigger	Yes	No	No
Cutaneous trigger	No	No	Yes
Indomethacin effect	-	Absolute response	-
Key treatment options			
Abortative	Sumatriptan (nasal, SC) Oxygen (high flow)	Nil	IV Lignocaine
Preventative	Verapamil Methysergide Lithium Steroids (short-term)	Indomethacin	Lamotrigine Topiramate Gabapentin

SUNCT / SUNA: rare TACs with short-duration attacks of unilateral head pain

- Autonomic features in both:
  - In SUNCT these include significant tearing and conjunctival injection,
  - In SUNA There is no significant tearing or conjunctival injection
  - However these conditions are clearly part of the same spectrum.
- The main differential is trigeminal neuralgia.
  - Pain in SUNCT/SUNA is typically in the ophthalmic division (rare for trigeminal neuralgia)
  - Autonomic features favour SUNCT/SUNA, of course.
  - Cutaneous triggers of pain paroxysms are often a feature of trigeminal neuralgia and also of SUNCT/SUNA
- The pain of SUNCT/SUNA may be short-lived single stabs (5-240 seconds), groups of stabs, or a saw-tooth pattern where the pain does not return to baseline between stabs and the attack lasts several minutes.
- There is no response to indomethacin (compare with paroxysmal hemicrania) or to the typical relievers for cluster headache.
- The most effective treatment is lamotrigine, with some efficacy also for topiramate and gabapentin.
- Ten days of IV lignocaine may also induce a remission.

Paroxysmal hemicrania

- Paroxysmal hemicrania comprises:
  - short attacks (lasting 2 to 30 minutes) recurring several times a day
  - of severe unilateral pain , typically in the ophthalmic division,
  - with associated autonomic features
  - There is often associated unilateral photophobia and phonophobia, and
  - restlessness and agitation.
- The attacks usually occur during the day, and a small percentage are triggered by alcohol or a manual trigger, such as head movement, pressure on C4 or C5, the C2 root or the greater occipital nerve. There are no cutaneous triggers, such as seen in SUNCT/SUNA.
- Paroxysmal hemicrania may be episodic (with remissions lasting more than one month) or chronic (with no remission in one year).
- There is a lasting response to indomethacin;
- In patients intolerant to the gastric effects of indomethacin, the alternatives are less clearly defined.
  - COX-2 inhibitors, topiramate and greater occipital nerve block with lidocaine and methylprednisolone acetate may be beneficial (all off label uses).

Hemicrania continua

- Hemicrania continua is a continuous side-locked headache of varying intensity.
- Exacerbations may be accompanied by ipsilateral autonomic symptoms, as well as migrainous features (nausea, photophobia, phonophobia).
- The background pain in hemicrania continua is greater than the interparoxysmal pain in the other TACs, and the exacerbations longer
- **There is a complete resolution of the headache with therapeutic doses of indomethacin, which is one of the diagnostic criteria.**
- An oral indomethacin test may be performed using a regimen of 25 mg thrice daily for one week, increasing to 50 mg thrice daily in the second week and 75 mg thrice daily in the third. Prophylactic use of a proton pump inhibitor is advisable to reduce gastrointestinal complications.
- If the test is positive, the dose can be gradually decreased until the minimal effective dose is established.
- As with paroxysmal hemicrania, topiramate, greater occipital nerve block and occipital nerve stimulators have all been reported to be beneficial.

Primary stabbing headache

- Primary stabbing headache has been called ‘jabs and jolts’ or the graphic term ‘ice-pick pains’ with which patients readily identify, as the pain is often described as being like a very local and very brief stab into the head.
- The pain occurs spontaneously (unprovoked) and is predominantly felt in orbital, temporal or parietal area). Stabs last for up to a few seconds and recur with irregular frequency ranging from one to many times per day. The stabs are often confined to one area, but in some patients they may move about the head, including to the opposite side. Usually there are no accompanying symptoms such as nausea, light sensitivity or autonomic changes. Findings on examination (and imaging, if performed) are normal.
- This condition is not rare; many patients do not bother to mention it. Others are concerned that it represents serious pathology and are reassured by a definite diagnosis. Only rarely do patients find it disabling and most do not require treatment.
- Many patients with primary stabbing headache have migraine as well: if so the pains are felt predominantly on the side most affected by these headaches.
- Differential diagnoses would include brief forms of TAC such as SUNCT and paroxysmal hemicrania, but these would typically have associated autonomic symptoms.
- A positive response to indomethacin has been reported in some uncontrolled studies, but others have found partial or no response.

Cough headache

- Cough headache is a headache of sudden onset, lasting from one second to 30 minutes, brought on by, and occurring only in association with, coughing, straining and/or the Valsalva manoeuvre.
- Typically, the headache is bilateral, very abrupt in onset and immediately at maximum severity. The severity then decreases gradually over 15 to 30 seconds, often with a pulsatile quality during this time.
- In about 40% of cases there is demonstrable obstruction to CSF flow at the foramen magnum; the most common such cause is Chiari malformation.
- This makes sense as the headache can be explained by failure of intracranial and intraspinal pressures to equilibrate immediately (as they normally do) after coughing or straining when raised intrathoracic pressure is transmitted through the venous system to the intracranial cavity. A pressure gradient across the foramen magnum will cause pain from traction on meninges, vessels and other pain-sensitive structures. The pain wanes as pressures gradually equalise.
- Cough headache obviously mandates careful imaging of the brain, and the region of the foramen magnum in particular. MRI provides excellent views of this area, but the radiologist must be alerted that this is the area of interest.
- Patients with no abnormality on imaging are classified as having ‘primary cough headache’, formerly called ‘benign cough headache’. Radiologically inapparent obstructions at the foramen magnum may account for some of these cases. (I have one case in which the symptoms were relieved after surgical exploration of the region showed fine bands of arachnoid tissue that were then cleared away.)
- Cough headache often responds to indomethacin, at least to some extent, but this may occur both in ‘primary’ cases and in those with demonstrable obstruction, so the response is not of diagnostic value.

Primary exertional headache

- Primary exertional headache, also called benign exertional headache, is probably heterogeneous.
  - Migraine may also be provoked by exertion (or perhaps by the associated fluid depletion).
  - Some exertional headache is explosive in onset and is triggered by sudden straining or the Valsalva manoeuvre (for example with weightlifting) and thus has similarities to orgasmic headache and cough headache.
  - Other cases develop more gradually in response to more prolonged exertion.
- Some degree of exertional headache is not rare. One survey found 30% of adolescents reported headache during or following exertion.
  - The headaches were often bilateral, pulsating and brief (lasting less than an hour).
  - Migraine predisposed to exertional headache, with 47% of those with migraine reporting it compared with 21% of those without.
- The pathophysiology of primary exertional headache is unknown. One group has postulated that excessive transmission of venous pressure to the intracranial space following Valsalva-like manoeuvres may contribute. They found internal jugular vein valve incompetence using duplex ultrasound in 70% of patients with exertional headache and 20% of controls.

Hypnic headache

- Hypnic headache is a rare primary headache disorder
- It occurs mainly in older patients (average age of onset is about 60)
- Exclusively sleep-related headache attacks.
- The headache may be unilateral or bilateral and is usually severe or at least moderately severe.
- The headache attacks are very disruptive as they typically occur once or twice each night and most patients have to get up and move about
- Some patients then drink coffee as caffeine appears to provide some relief. Many patients do not discover coffee as it is counter-intuitive (They assume it might keep them awake and disturb sleep even more)
- Prophylactic treatments include coffee before going to bed (which in fact in these patients rarely prevents sleep)
- Also reported anecdotally are lithium, topiramate, indomethacin, melatonin and amitriptyline (off label uses).

Holle D, Naegel S, Krebs S, Katsarava Z, Diener HC, Gaul C, Obermann M. Clinical characteristics and therapeutic options in hypnic headache. Cephalalgia 2010, Dec;30(12):1435-42.

Nummular headache

- Nummular headache is a rare primary headache disorder in which there is a focal 'coin-shaped' circumscribed area of pain, 2 to 6 cm in diameter
- From the Latin *nummulus,* a small coin
- Nummular headache is typically persistent in type with some superimposed exacerbations of more severe pain (which is still usually described as a dull ache). There is only rarely sharper pain or local tenderness.
- No treatment is reliably effective.
- There is an anecdotal report of benefit from botulinum toxin injection in a small number of patients (off label treatment).
- The natural history is very variable: some cases resolve spontaneously but others may continue for years.

Moon J, Ahmed K, Garza I. Case series of sixteen patients with nummular headache. Cephalalgia 2010, Dec;30(12):1527-30.
Mathew NT, Kailasam J, Meadors L. Botulinum toxin type A for the treatment of nummular headache: Four case studies. Headache 2008, Mar;48(3):442-7.

Exploding head syndrome

- Sufferers describe alarming attacks of a painless explosion within their head. Attacks tend to occur at the onset of sleep, even at the start of day-time naps.
- This condition is probably not rare: when Pearce first described 10 cases with this evocative name, it received substantial press coverage and he was then inundated with correspondence describing similar cases, so that within a year he could publish a review of 50 well documented cases
- The cause is uncertain but the timing suggests a similarity to the other physiological phenomena such as nocturnal myoclonus, which mark the transition from wakefulness to stage 1 sleep.
- No reliable treatment is known but clomipramine has been suggested anecdotally.

Pearce JM. Clinical features of the exploding head syndrome. J Neurol Neurosurg Psychiatry 1989, Jul;52(7):907-10.

A clinical approach

- Consider tempo
  - Thunderclap
  - Acute
  - Recurrent
    - Timing / Episodic nature
- Exclude secondary causes
- Is it a TAC?
- Is there a typical provoking cause?