Headache Update

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Disclosures

I have received funding from the following companies for providing educational sessions, attending advisory and editorial boards and received travel grants to attend conferences:

- Teva
- Allergan
- Continuum journal
- Novartis

CASE 1

35 year old female

Presents to neurologist with headache

Patient has googled her disorder

Neurologist disagrees with Google

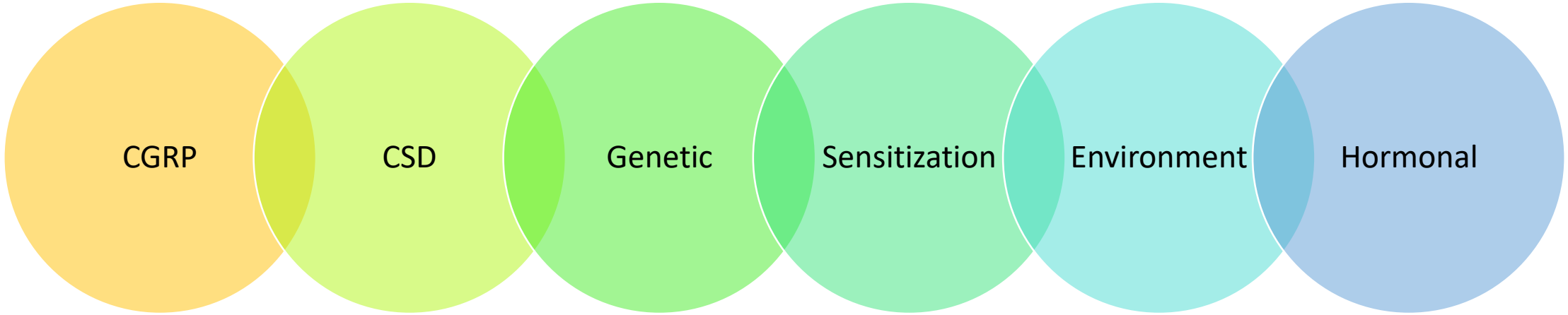
Symptoms

- 2 year history
- Headache
- Photophobia
- Phonophobia
- Neurologist- Migraine

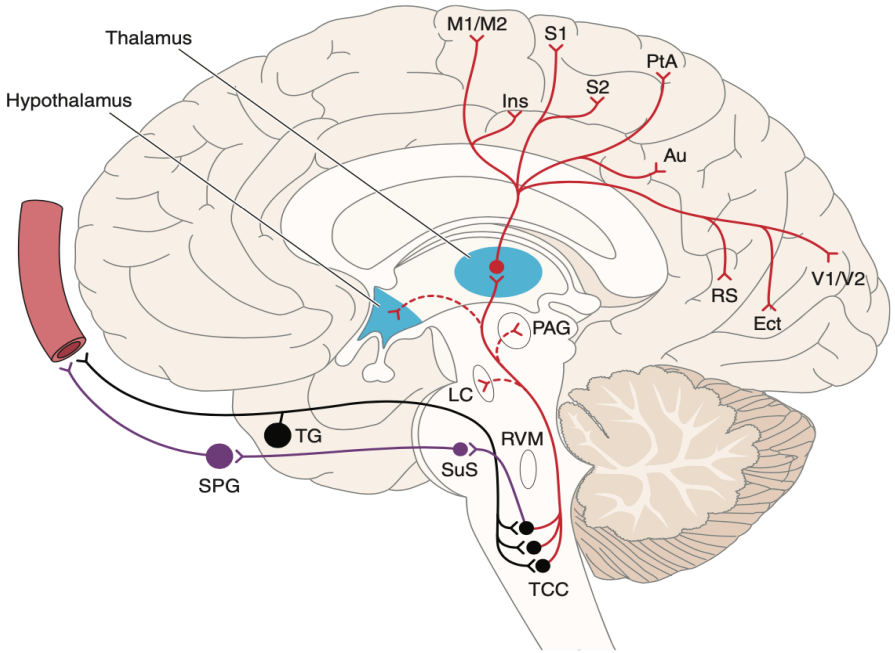
- Migraine- 12% general population[1]
- Migraine is more prevalent than diabetes, epilepsy and asthma combined[2]
- Costly
- NZ- 3431 discharges Migraine (others- 592)[3]
- Majority 20-49 age group
- Maori - 497 migraine discharges

- [1]Lipton *et al.,* Headache. 2001
- [2]Natoli JL *et al.,* Cephalalgia. 2010
- [3]Ministry of Health NZ data 2016/17

Primary neuronal dysfunction



CGRP- Calcitonin gene related peptide
CSD- Cortical spreading depression
Genetic- FHM1,2,3, TRESK
Hormonal- Serotonin, Oestrogen



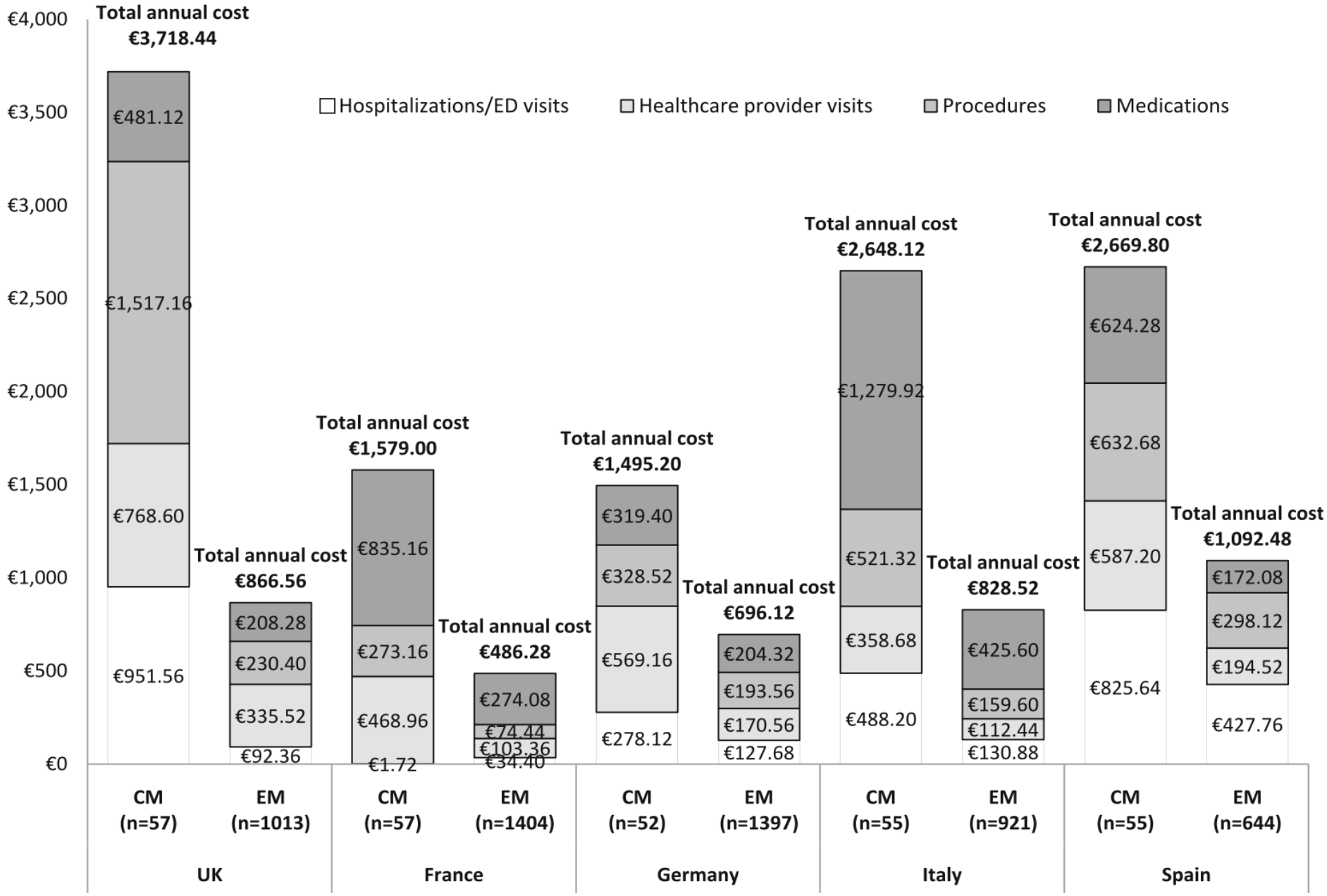
Burden

Second most disabling[1]

Substantial negative impact on patients' lives and their familial, social, and professional environment[2]

Cost- US 17 Billion $ per year[3]

[1]Global burden of disease Lancet 2017
[2]Patient perceptions of the impact and burden of migraine: an international survey of 12,545 patients across 16 countries- MTIS 2020
[3]Goldberg. The cost of migraine and its treatment. Am J Manag Care. 2005



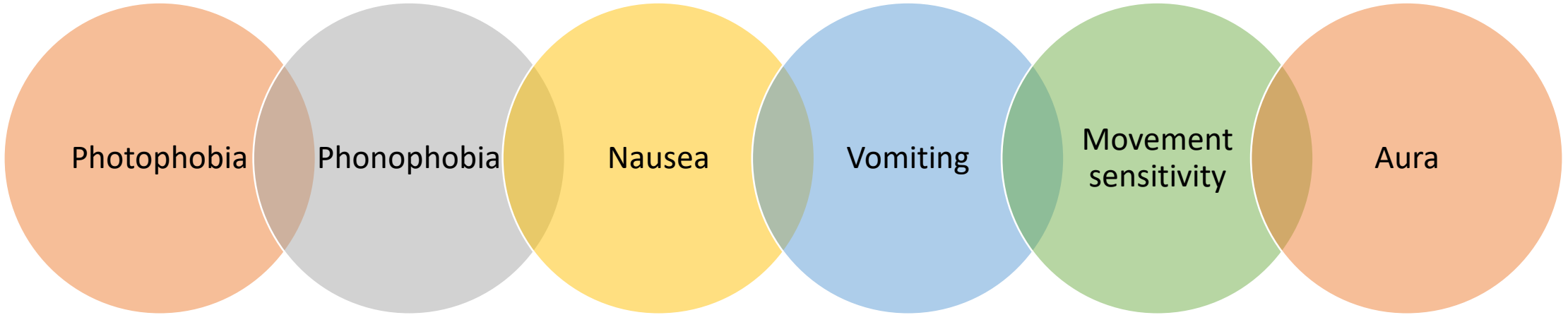
J Headache Pain (2012)

Presenting symptoms

- Number of headache days out of 30 per month
- Crystal clear days[1]
- Site/Character/Duration
- Circadian/Circannual periodicity[2]
- Thunderclap?
- Valsalva
- Postural variation

[1]Khalil *et al.,* Prospective analysis of the use of Onabotulinumtoxin A (BOTOX) in the treatment of chronic migraine J Headache Pain. 2014
[2]May A. Cluster headache: pathogenesis, diagnosis, and management. Lancet. 2005

Associated features



Unilateral photophobia or phonophobia in migraine compared with trigeminal autonomic cephalalgias

206

Episodic migraine - 4%

Chronic Migraine - 13%

Chronic Cluster headache - 48%

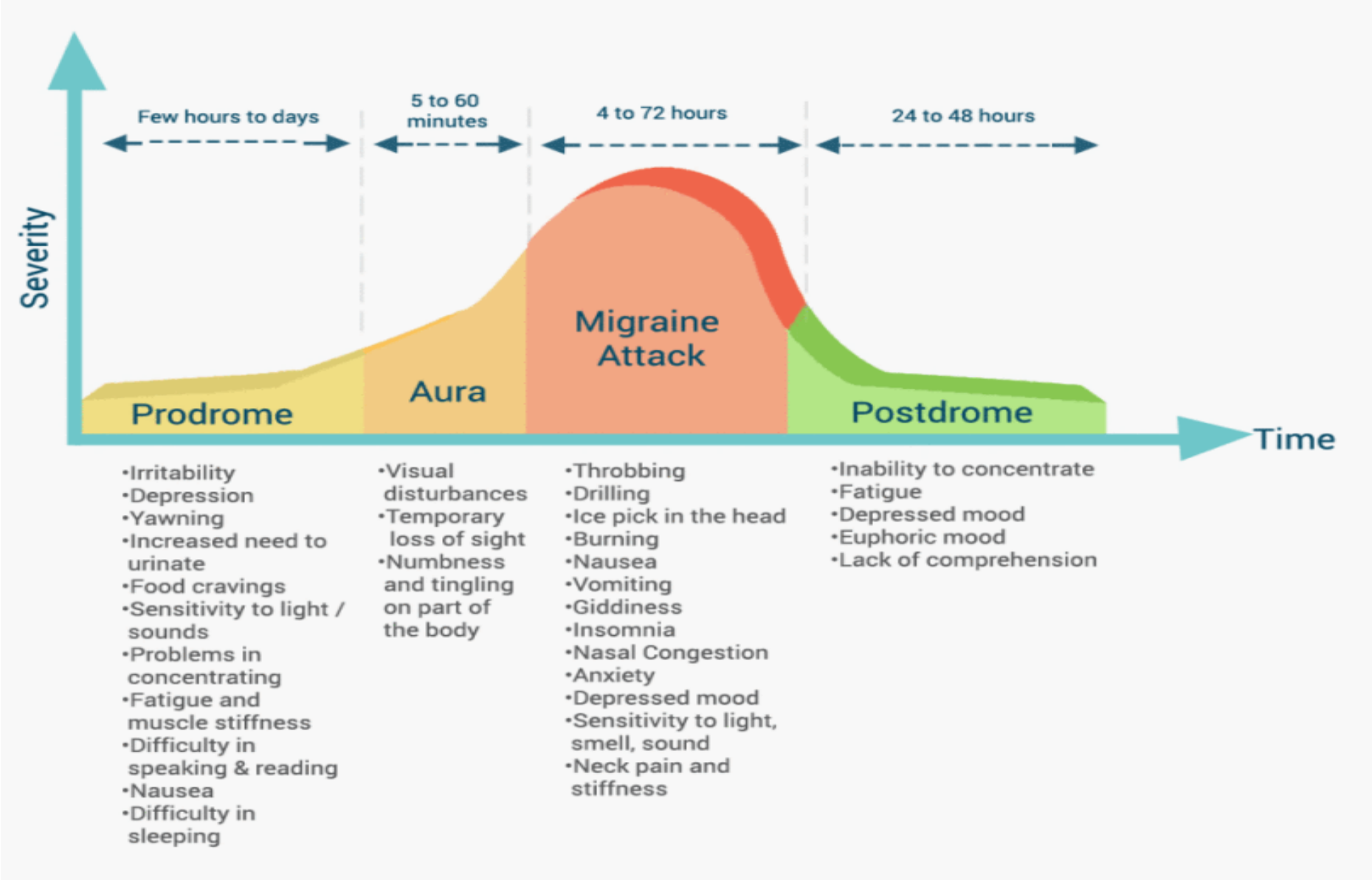
Episodic cluster headache - 80%

Hemicrania Continua- 56%, SUNCT- 56%

Lateralization > in TACs than migraine ($\chi^2 = 84.9$, $P < 0.0001$)

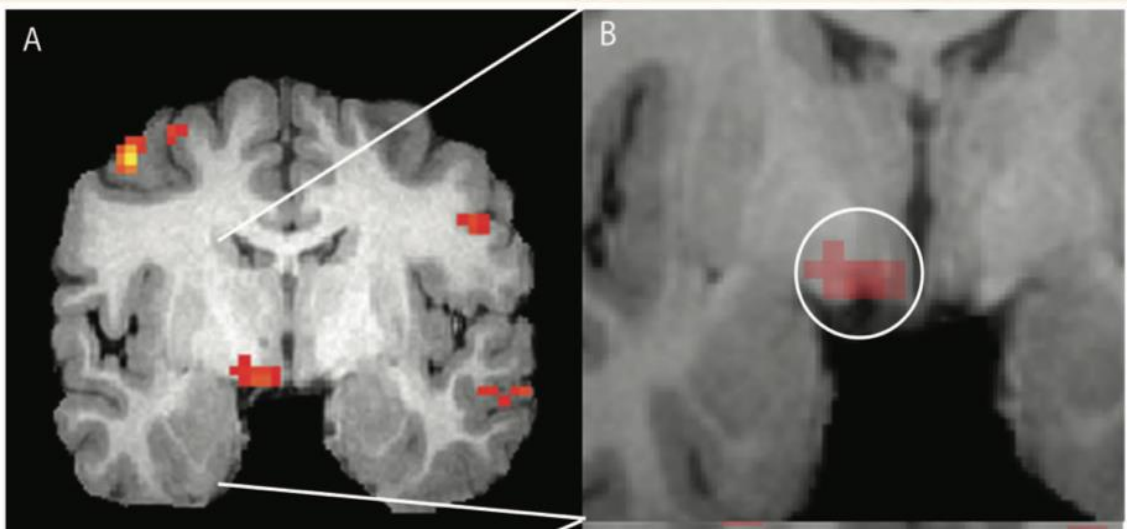
Irimia P *et al.,* Cephalalgia. 2008

Migraine phases



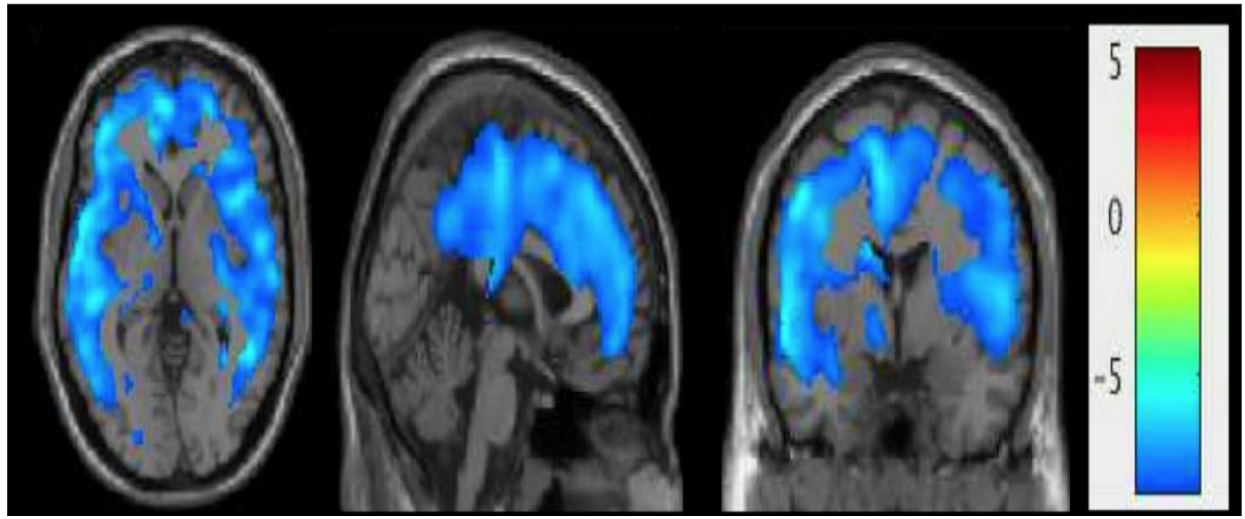
FUNCTIONAL IMAGING

- Premonitory (Prodrome)



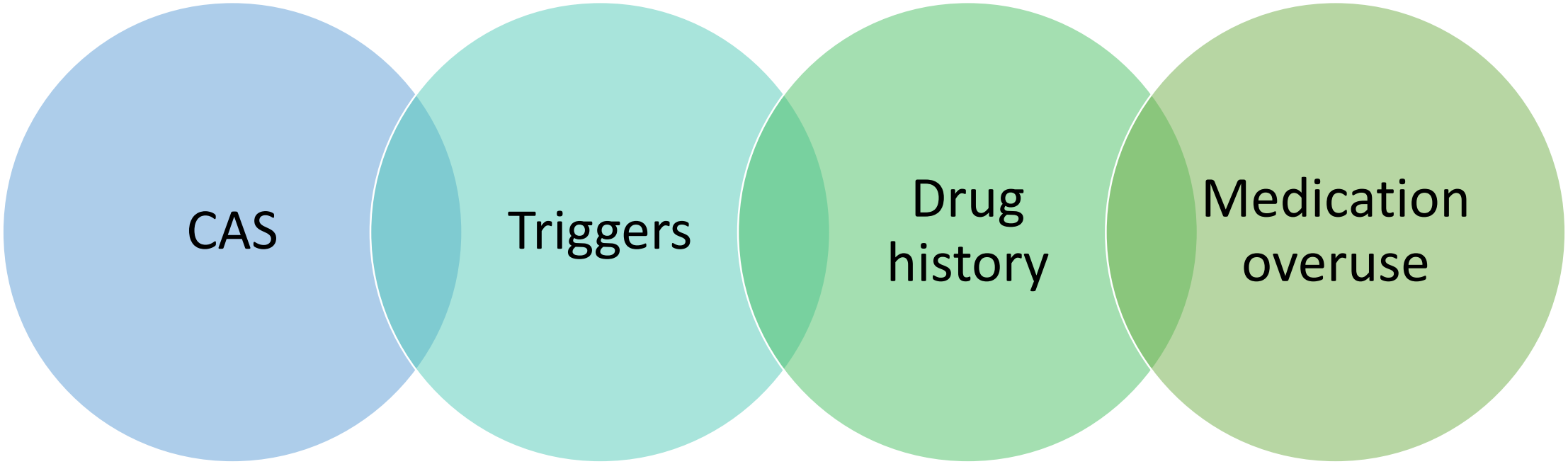
Maniyar *et al.,* Brain. 2014

- Postdrome



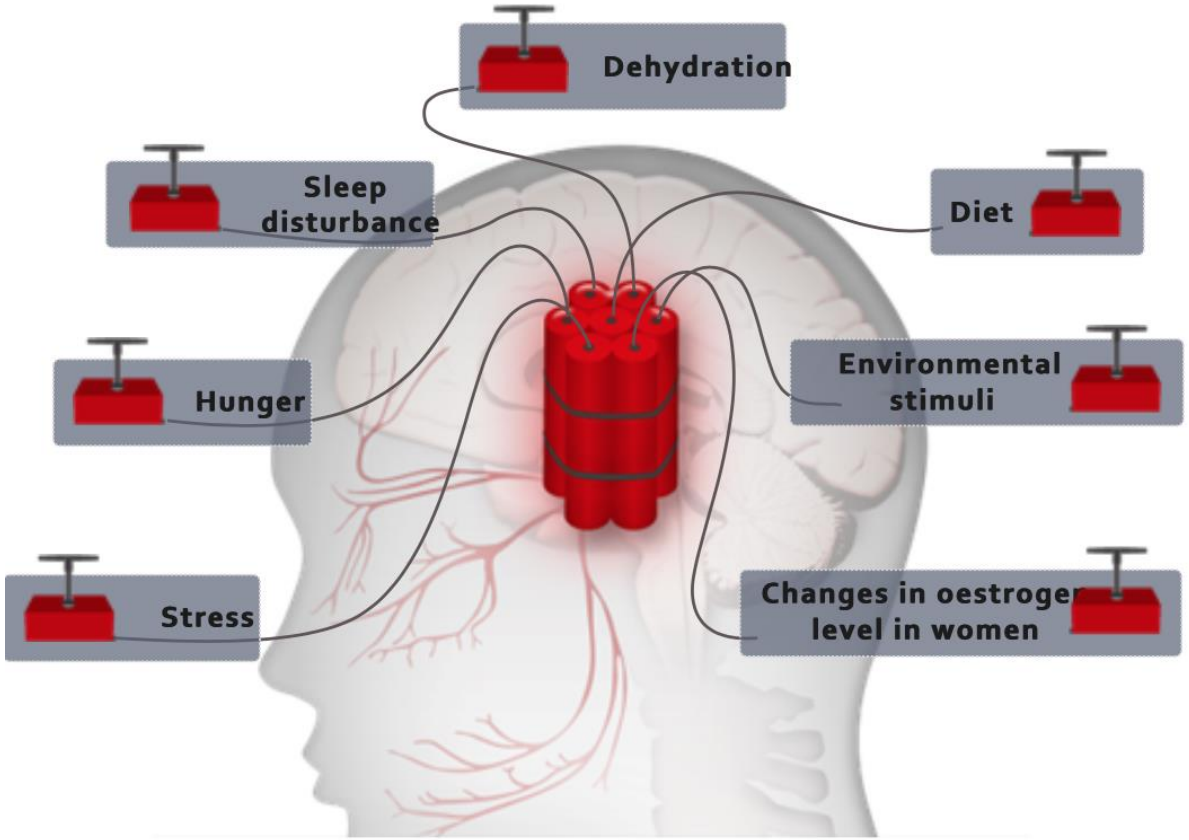
Bose *et al., JNNP* 2017

OTHERS



CAS (Cranial autonomic symptoms - ptosis/red eyes/watering/rhinorrhea)
Drug History- ? Max dose of preventives/ ? Side-effects
Medication overuse– Paracetamol/NSAIDS 15/30, Opiates- 10/30, Triptans 10/30

TRIGGERS


Dehydration
Sleep disturbance
Diet
Hunger
Environmental stimuli
Stress
Changes in oestroge level in women

Examination

- Changes to behavior/personality
- Confusion
- Papilledema
- Ophthalmoplegia
- Focal neurological deficits

RED FLAGS- SNOOP

- **S**ystemic symptoms including fever
- **N**eoplasm history/Neurological deficit
- **O**nset sudden, **O**lder age (onset after age 50 years)
- **P**attern change, **P**recipitated by sneezing, coughing, or exercise
- **P**rogressive headache, **P**regnancy or puerperium
- **P**ainful eye with autonomic features
- **P**athology of the immune system such as HIV

Red and orange flags for secondary headaches in clinical practice: SNNOOP10 list. Do et al., Neurology. 2019

CASE 1

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Symptoms

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- Neurologist- Migraine

Symptoms

- 2 year history
- Headache- Right sided retro-orbital

Sharp/piercing pain

Lasts around 1 hour

Usually at 2 am

With unilateral cranial autonomic symptoms

Lasts 6-8 weeks

Completely symptom free in between.

- Photophobia- Right sided
- Phonophobia- Right sided

MIGRAINE

- >5 attacks
- 4-72 hours
- 2 of (unilateral, pulsating, moderate to severe, aggravation with activity)
- Nausea/Vomiting
- Photophobia/Phonophobia

ICHD-3 Criteria

Cluster Headache

- ‘Suicide headaches’
- >5 attacks
- Very severe unilateral orbital/supraorbital/temporal pain
- 15-180 mins
- Ipsilateral cranial autonomic symptoms
- Restlessness or agitation during attacks

ICHD-3 Criteria

*Migraine Management – Acute (Non-triptan)

Drug	Dose	Max dose 24 hours
Paracetamol	1000 mg	4000 mg
Ibuprofen	400-600mg	2400 mg
Aspirin	600-1000 mg	4000 mg
Naproxen	250-500 mg	1000 mg

* Based on RCT data / At least 2 international treatment guidelines

*Migraine Management – Acute (Triptans)

Drug	Dose	Max dose 24 hours
Sumatriptan oral Sumatriptan injection	50-100 mg 6mg	300 mg 12 mg
Rizatriptan**	10 mg	20 mg
Zolmitriptan nasal spray	5 mg	10 mg

* Based on RCT data / At least 2 international treatment guidelines

**Drug interaction Rizatriptan/Propranolol- use 5 mg instead

Preventives- Episodic and Chronic Migraine

Drug	Dose	Titration	Trial Study dose
Amitriptyline	10-25 mg	10-25 mg	25-150 mg
Propranolol	10 mg BD	10-20 mg	120-240 mg
Topiramate	25 mg	25 mg	25-200 mg
Candesartan	2 mg	2 mg	8-16 mg
Botox*	155 u every 3/12		

Based on RCT data / At least 2 international treatment guidelines
Sodium valproate/Pizotifen- weight gain
*Chronic migraine

CGRP Monoclonal Antibodies

Commercial Name	Eptinezumab ALD403	Erenumab AMG334	Galcanezumab LY2951745	Fremenezumab TEV-48125
Type	Humanised Yeast	Human Murine	Humanised Murine	Humanised Murine
Trials	Promise 1 (E) Promise 2 (C) Prevail (OL LT)	Arise & Strive (E)	Evolve 1 & 2 (E) Regain (C) Conquer ©	Halo (E) Halo (C) Focus (OL LT)
Against	CGRP	Receptor	CGRP	CGRP
Route/Dose	IV every 12 weeks	SC every 4 weeks	SC every 4 weeks	SC every 4 weeks
Studies	Migraine	Migraine	Migraine Cluster	Migraine Cluster

Cluster headache – Acute Treatment

- High Flow oxygen 15L/min- nonrebreathing facial mask
- Sumatriptan injection
- Avoid oral triptans

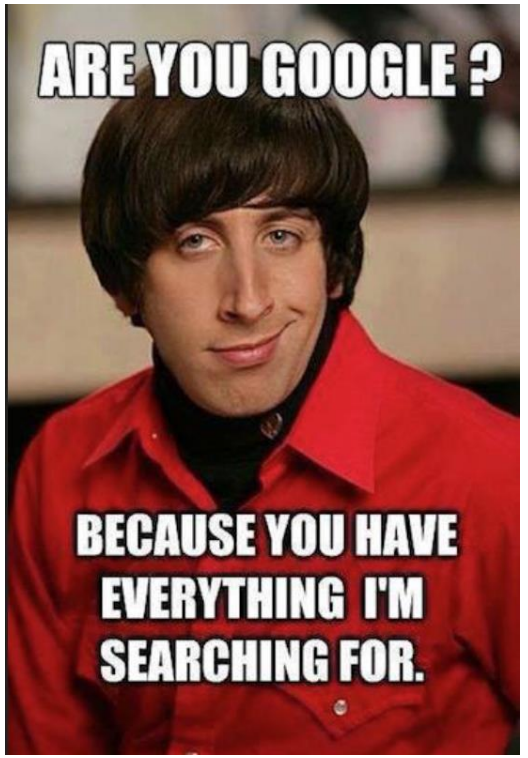
Cluster Headache - Preventives

Drug	Dose	Titration	Max dose
Verapamil	80 mg TDS	80 mg	960 mg
Topiramate	25 mg OD	25 mg	200 mg
Prednisolone	60mg OD- 5 days	Reduce by 10mg/day	10-day course
Greater occipital nerve block	Methylpred-80mg Lignocaine 2%		

Based on RCT data / At least 2 international treatment guidelines
Sodium valproate/Pizotifen- Limited evidence
Lithium – narrow therapeutic window
Galcanezumab – CGRP monoclonal antibody

KEY POINTS FROM THIS CASE

- Cluster headache is still commonly missed[1]
- Unilateral photo/phonophobia can be helpful
- Artificial intelligence is getting smarter



[1]Cluster headache. Nesbitt AD, Goadsby PJ.BMJ. 2012

CASE 2

68 yr old female

On holiday in Spain

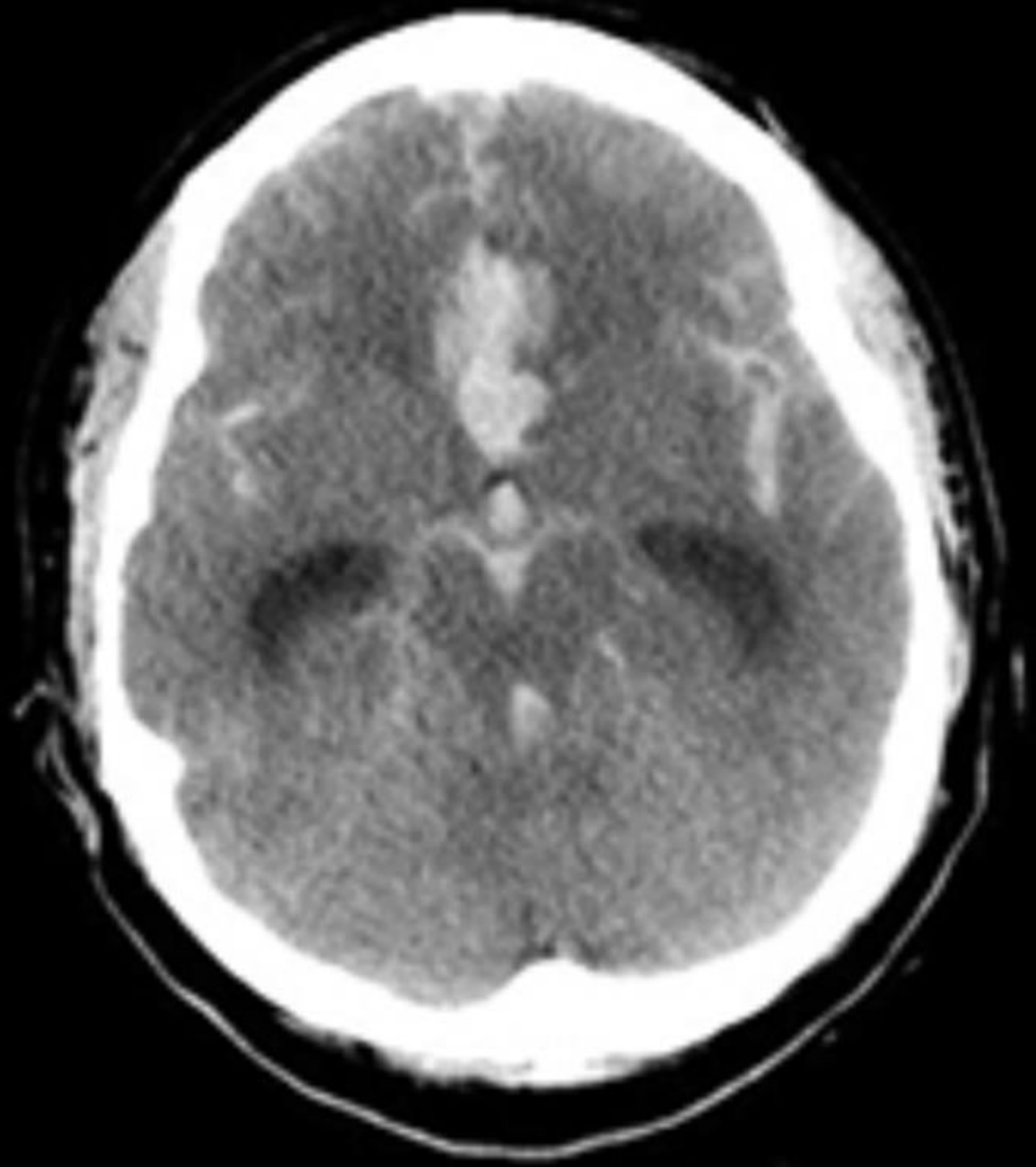
Sunbathing at onset of headache

Abrupt onset of headache

Left occipital region, throbbing, photophobia, lightheaded

ED in Spain – diagnosed migraine and discharged with analgesia

Represented to ED in UK



Subarachnoid Haemorrhage

- Thunderclap headache (sudden explosive, pain peaks in 1 min or less)
- ‘Worst ever’
- CT head (98% <6 hours)
- CSF Xanthochromia – After 12 hours
- 1 in 20 missed in Emergency department
- Common reason neurologists sued!

Thunderclap Headache

- Subarachnoid haemorrhage
- Cervical arterial dissection
- Cerebral venous sinus thrombosis
- Pituitary apoplexy
- Spontaneous intracranial hypotension
- Reversible cerebral vasoconstriction syndrome (RCVS)
- Stroke

CASE 3

- 57 yr female
- 3-month history throbbing headaches/photophobia/phonophobia (Migraine)
- 5 days before presentation- weakness right upper limb - 10 minutes followed by frontal headache - 5 minutes
- Admission day- weakness left upper limb – 10 minutes

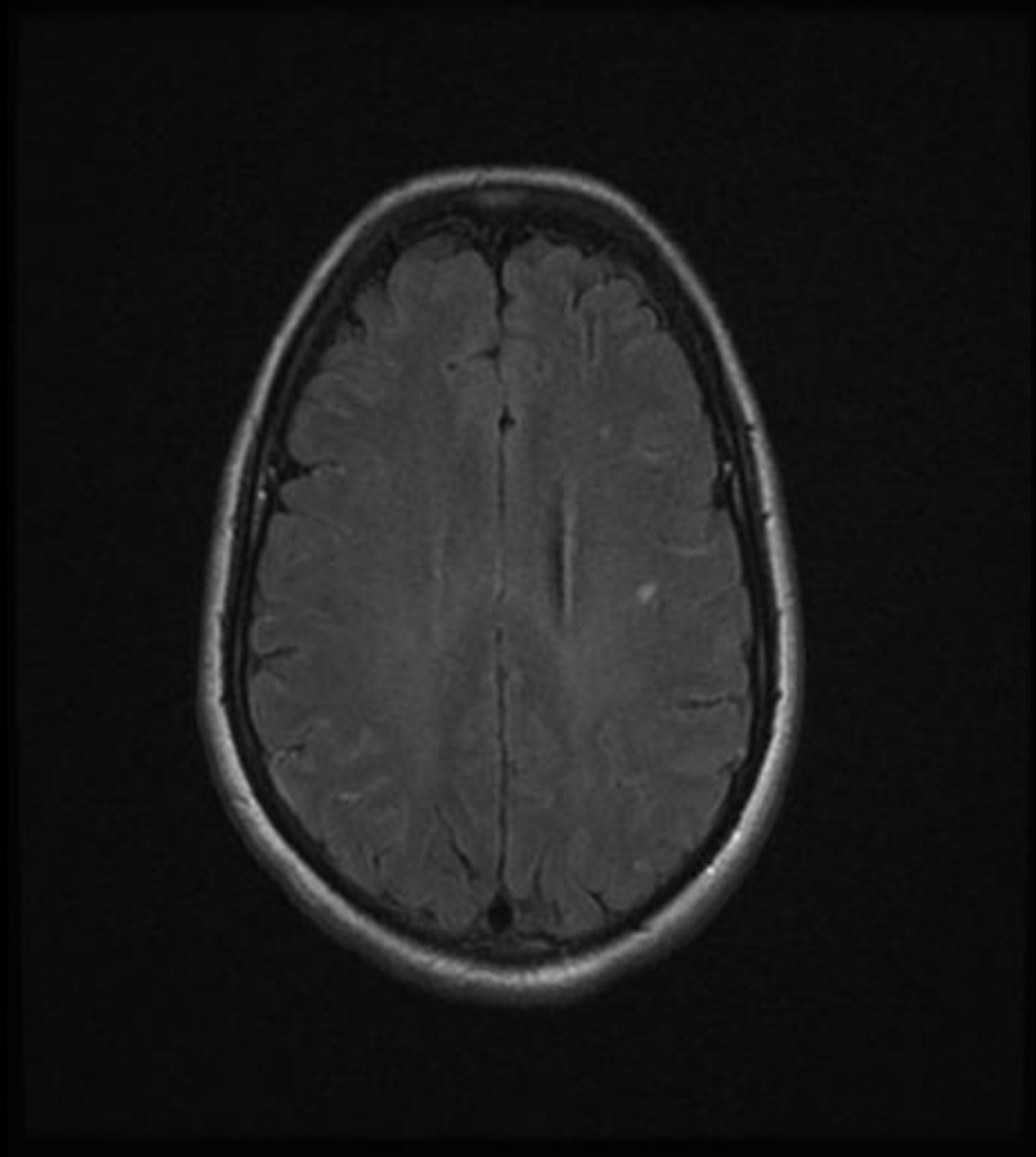
MEDICAL TEAM

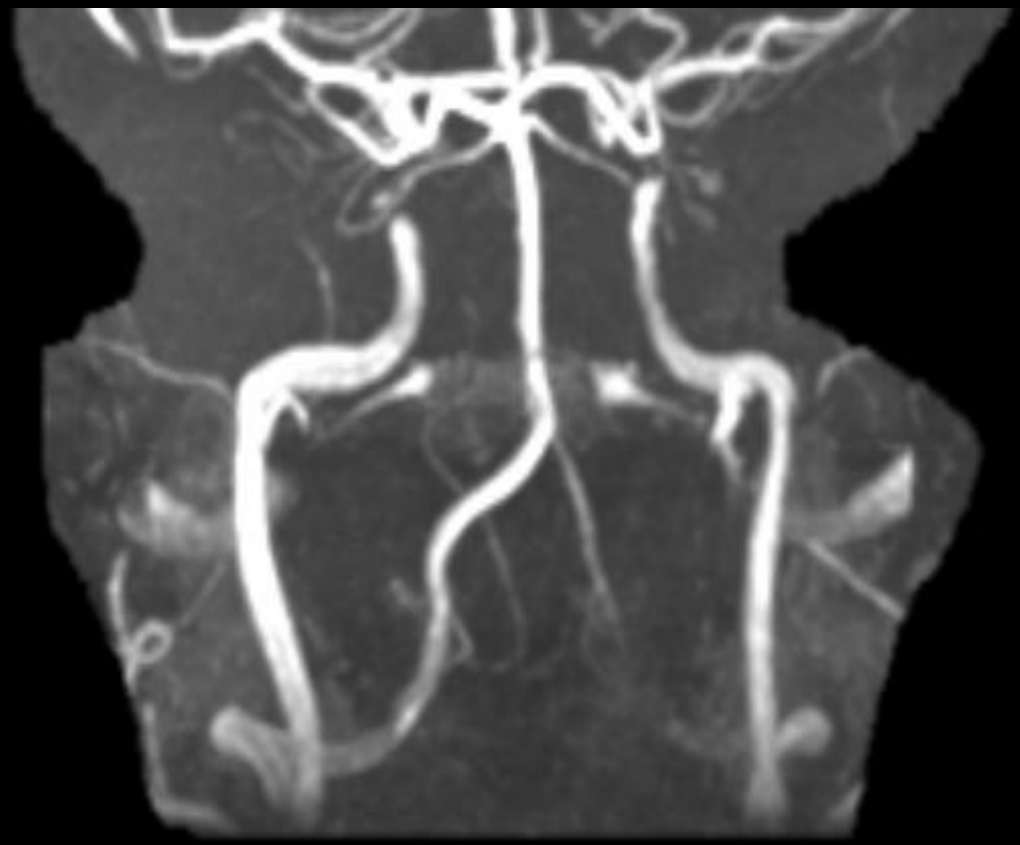
- Afebrile
- BP 134/90
- Completely normal neurological examination
- CT head reported as normal
- Medical Team- ? Transient Ischaemic attack ? Migraine
- Full blood count, Urea and electrolytes, CRP, Glucose
- Neurology Opinion

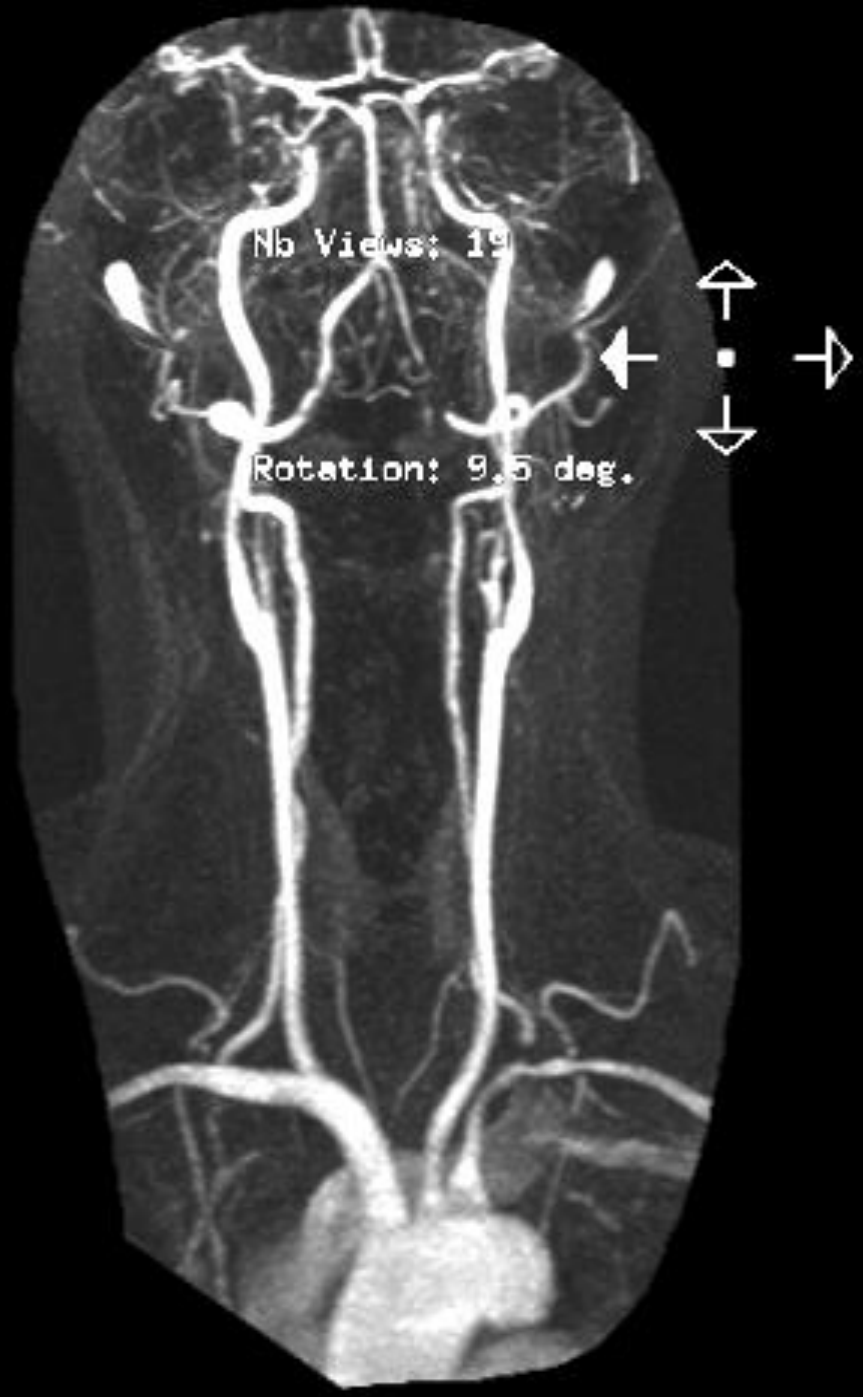
Neurology Review

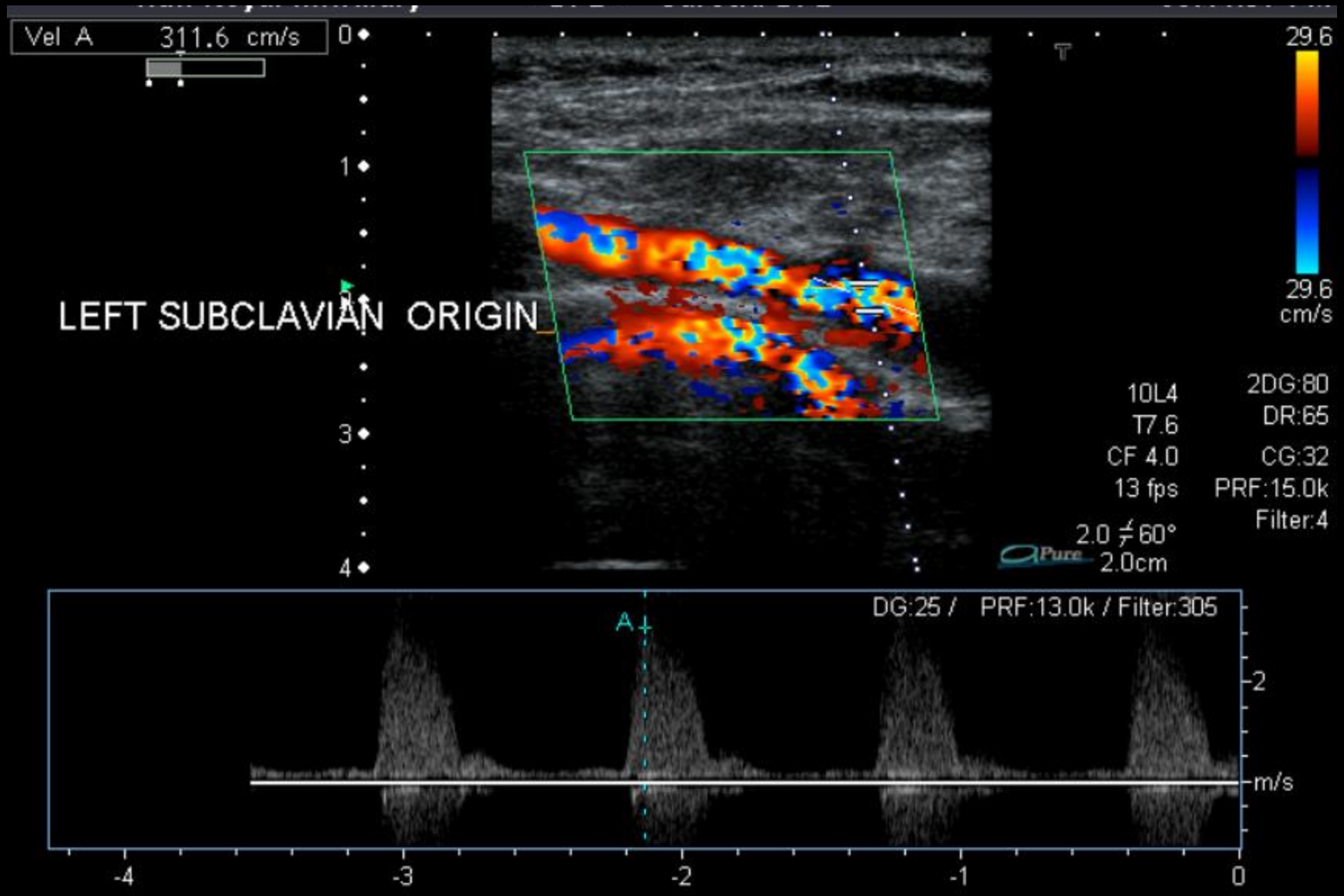
- All symptoms settled
- Patient keen to go home
- Left carotid bruit
- Harsh systolic cardiac murmur

- ESR, vasculitis screen
- Carotid Doppler
- Echocardiogram
- MRI Brain and MR Angiogram requested
- Started antiplatelets (? TIA)
- Admit under Neurology






Nb Views: 19
Rotation: 9.5 deg.


Vel A 311.6 cm/s
0
1
3
4
LEFT SUBCLAVIAN ORIGIN
29.6
29.6
cm/s
10L4
T7.6
CF 4.0
13 fps
2.0 ≠ 60°
2.0cm
2DG:80
DR:65
CG:32
PRF:15.0k
Filter:4
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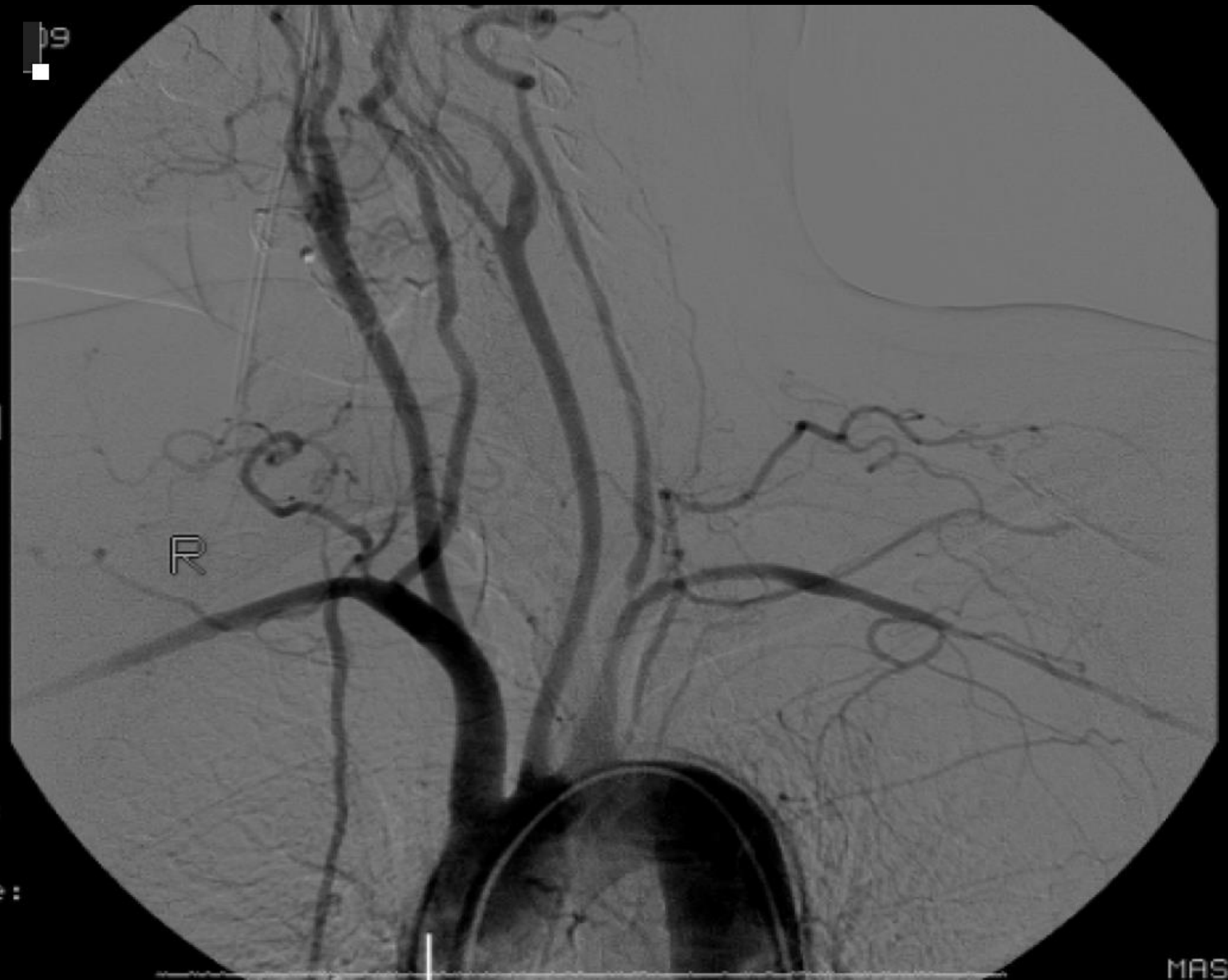
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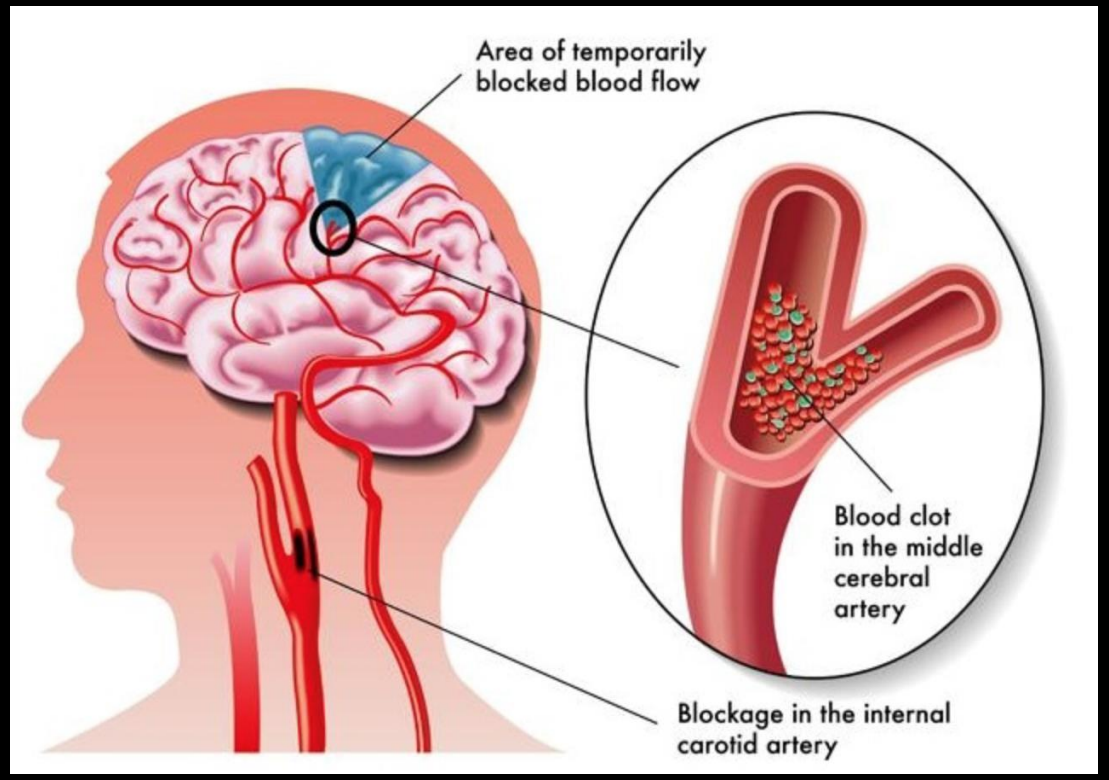
TAKAYASU'S ARTERITIS

- 1908 - Dr Mikito Takayasu
- Large vessel vasculitis
- Multisystem (joints, brain, heart, lung, gastro)
- Neurology - headaches, strokes

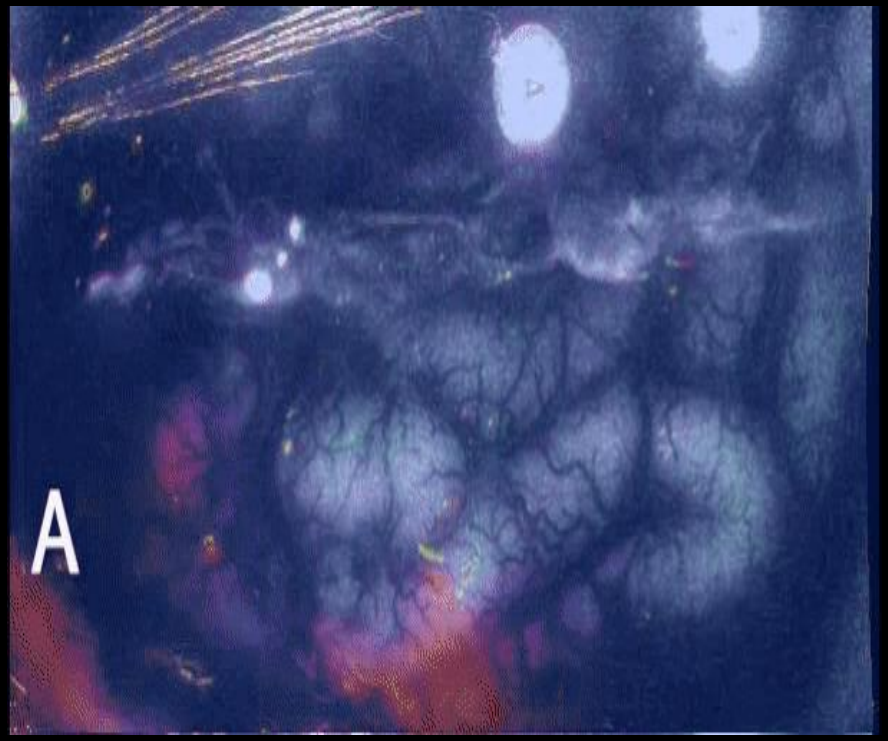
Differentiating between TIA/stroke and migraine with aura

TIA/Stroke	Migraine with Aura
Negative symptoms	Positive, then negative symptoms
All symptoms at onset	Gradual spread over minutes
Symptoms clear together in TIA	Symptoms may clear in one modality before onset of symptoms in another modality
Can affect more than one modality simultaneously	Spreads from one modality to another
Duration up to 30 min most common in TIA, but can last hrs; enduring deficits in stroke	20-30 min aura is most common, usually followed by headache
Usually >40 yrs old	Often begins in teens or twenties
Stroke risk factors present	Often a personal/family history of migraine

Adapted from Imitators of Epilepsy, 2nd Edition. Kaplan PW, Fisher RS, editors. New York: Demos Medical Publishing; 2005


Area of temporarily blocked blood flow
Blood clot in the middle cerebral artery
Blockage in the internal carotid artery

Stroke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CSD

Potential new neuropeptide targets

- CGRP
- PACAP- 38
- PACAP -27
- VIP
- AMY_1 receptor
- 5’-triphosphate sensitive potassium (KATP) channels
- Voltage-activated potassium (BK) channel

Dickenson *et al*., data presented at MTIS 2020

PACAP- Pituitary adenylate cyclase-activating peptide

VIP- Vasoactive intestinal peptide

AMY1- Amylin

TAKE HOME MESSAGES

- Headache is a common medical complaint
- Costly and major cause of disability
- Early diagnosis and management is key
- Novel treatments on the horizon
- https://aucklandregion.healthpathways.org.nz