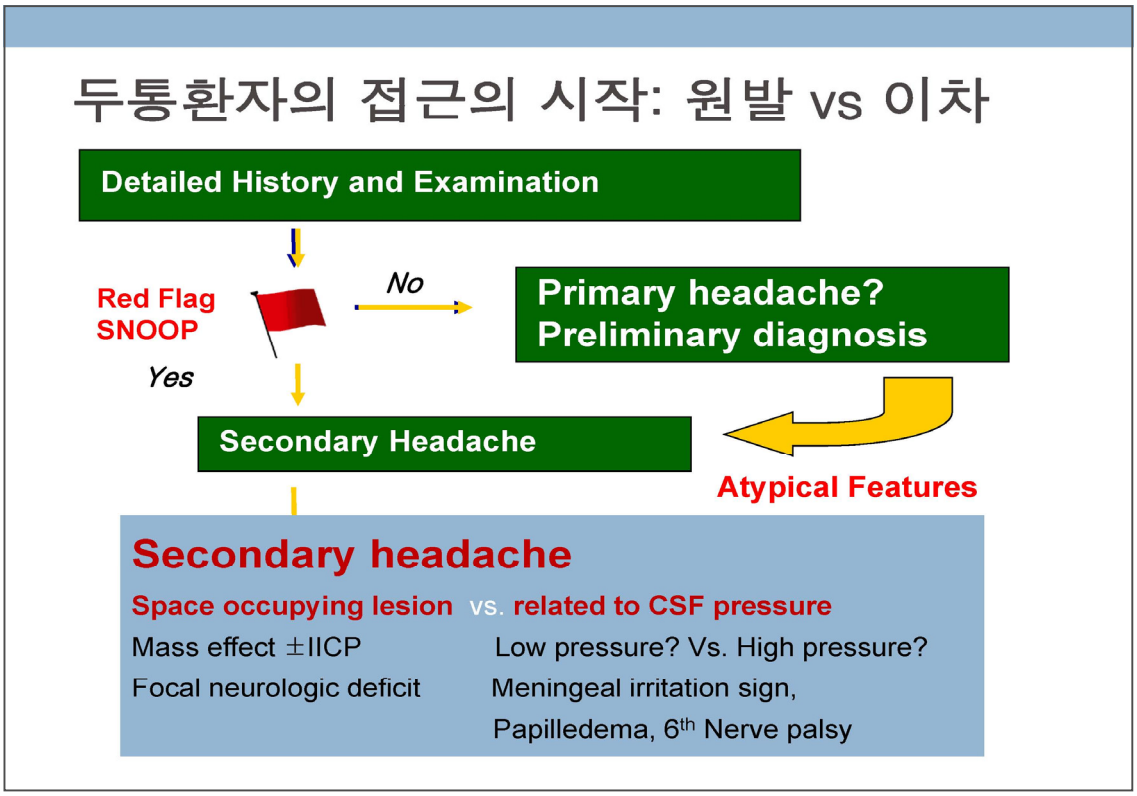
Migraine and other headache

문 희 수
성균관의대



Worrisome Headache Red Flags "SNOOP"

Systemic symptoms (fever, weight loss) or
Secondary headache risk factors (HIV, systemic cancer)
Neurologic symptoms or abnormal signs (confusion, impaired alertness, or consciousness)
Onset sudden, abrupt, or split-second
Older: new onset and progressive headache especially in middle age >50 (Giant cell arteritis)
Previous headache history or headache progression: first headache or different/change in attack frequency, severity or clinical features)

간헐적으로 반복되는 두통

Headache Classification and contents

Part 1
The primary headaches

Part 2
The secondary headaches

Part 3
Cranial neuralgias other facial pain and other headaches

Appendix

1. **Migraine**
2. Tension-type headache
3. Trigeminal autonomic cephalalgia
4. Other primary headache

✓A. at least five attacks fulfilling B-D.

✓B. Headache attacks lasting 4-72 hours

✓C. Headache lasting two of the following characteristics:

1. Unilateral location
2. Pulsating quality
3. Moderate or severe intensity
4. Aggravation by walking stairs or similar routine physical activity

✓D. During headache at least one of the following:

1. Nausea and /or vomiting
2. Photophobia and phonophobia.

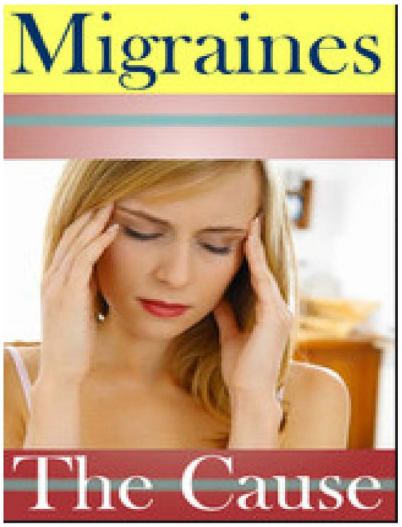
Why Is Migraine Mistaken For Other Headaches?

Mistaken For Tension-type Headache	
Neck Pain	75% migraine attacks
Stress	A common migraine trigger
Bilateral	40% migraine headache
Nonpulsating	50% of the time during migraine
Vomiting	<1/3 of migraineurs
Mistaken For Sinus Headache	
Weather changes	common migraine triggers
Tearing and nasal congestion	common during migraine attacks

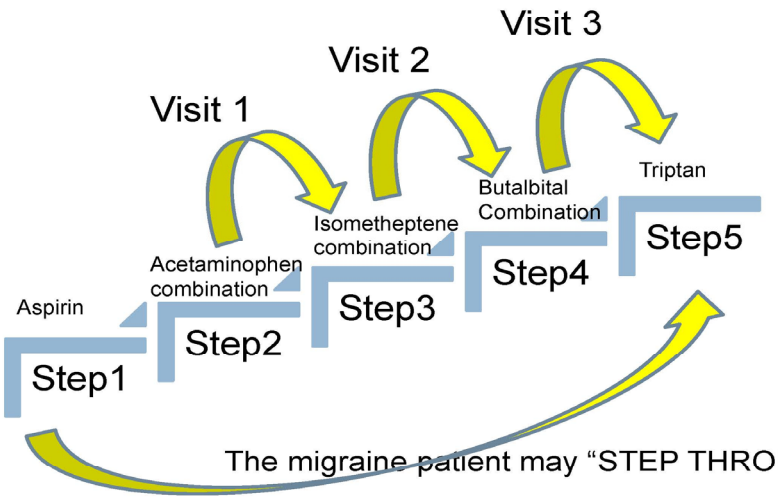
Recurring moderate-to-severe headache is migraine until proven otherwise

Migraine Additional Features

- Predictable timing around menstruation (or ovulation)
- Abatement with sleep
- Stereotyped premonitory symptoms
- Characteristic triggers (Wine, starvation)
- Positive family history
- Childhood precursors (motion sickness, episodic vomiting, episodic vertigo)
- Osmophobia



Step care vs. Stratified Care



The migraine patient may "STEP THROUGH" 4-6 therapies before finding one thath is effective

Lipton RB et al JAMA 2000:284;2599-2605

Key differences Ergot vs. triptan

	Ergots	Triptans	
5-HT			
1A	++++	+	Dysphoria/Nausea/Emesis
1B	+++	++	**Anti-migraine**
1D	+++	++	**Anti-migraine**
2A	+++	-	Peripheral vascular effects
2C	+++	-	Peripheral vascular effects
Adrenergic			
α1	+++	-	- Asthenia, - Dizziness
α2	+++	-	- Asthenia, - Dizziness
Dopamine			
D2	+++	-	GI/Nausea/Emesis

Which triptans?

DRUG	TIME TO PEAK LEVELS	ELIMINATION HALF-LIFE (HOURS)	BIOAVAILABILITY (%)	PRIMARY ELIMINATION
Almotriptan*	1.5–2 h	3.5	70	Renal 55%; CYP3A4 12%; MAOA 26%
Eletriptan	1.5–2 h	4	50	Hepatic, CYP3A4
Frovatriptan	2–4 h	26	22–40	Renal 38–49%; CYP1A2
Naratriptan	2–3 h	6	74 (f) 63 (m)	Hepatic, CP450/renal
Rizatriptan	1–1.5 h	2	40–45	Hepatic/renal
Sumatriptan oral	2–3 h	2	14	Hepatic, MAOA
Sumatriptan sc	12 min	1.9		Hepatic, MAOA
Zolmitriptan	1–1.5 h	2.5	40–46	Hepatic, MAOA

MAOA, monamine oxidase.
*Dahlof 2001.


이미그란
Sumatriptan

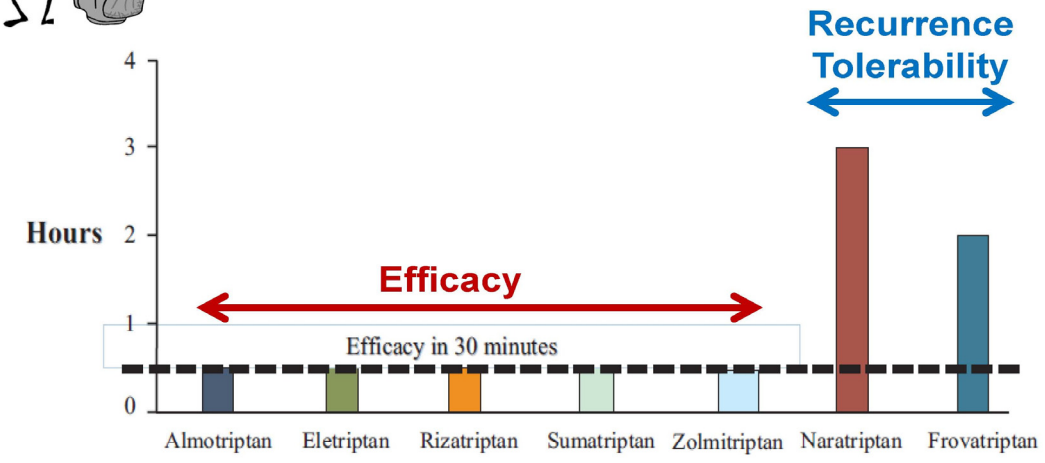

알모그란
Almotriptan


나라믹
Naratriptan


미가드
Frovatriptan

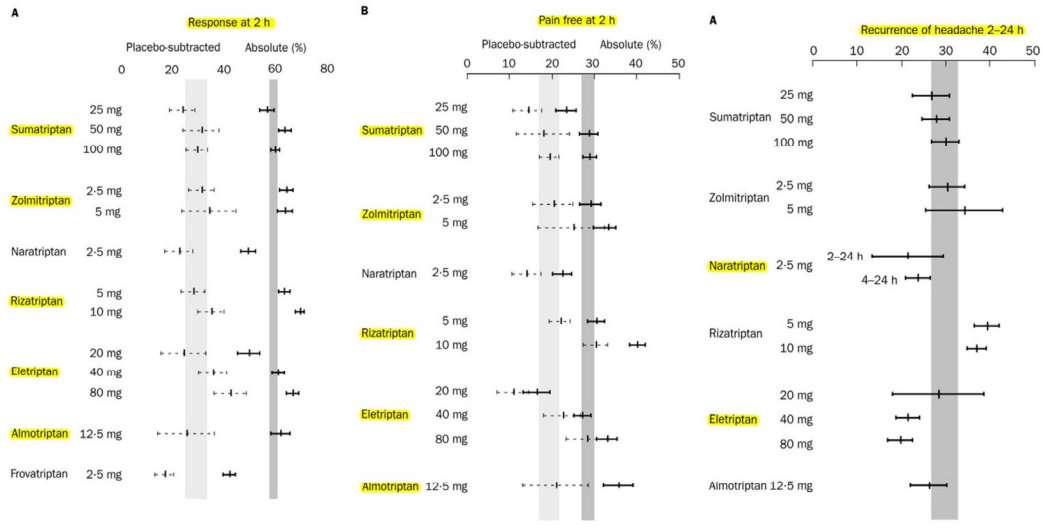

조믹
Zolmitriptan

Time to onset of efficacy of the oral triptans based on randomized controlled trials



Headache 2002, **42**, 99–113

Naratriptan, Frovatriptan 제외한 대부분의 triptan 2h pain response 60%, 2h pain free 30%.
Naratriatan, Frovatriptan은 24h recurrence rate가 낮음



증례

급격히 심해지는 편두통

잠에서 깰 때 이미 두통이 너무 심한 편두통

(1) 항구토제와 같이 빠른 효과 트립탄 (구토가 심하면 진통제 IM)

(2) 되도록 빨리 복용할 수 있게 하는 교육이 중요

트립탄을 복용해서 두통이 가라앉았는데 몇 시간 후에 다시 재발

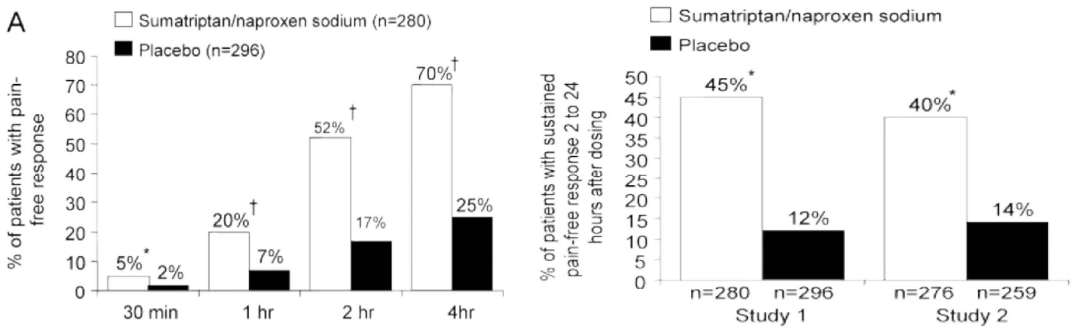
해결책:

(1) Naratriptan 또는 Frovatriptan 으로 변경

(2) Long acting NSAID(예. Naproxen) 를 기존의 트립탄에 추가

(3) 트립탄 복용하는 시점을 더 빨리 조정

Sumatriptan 85 mg + naproxen 500 mg RCT
2hr pain-free, recurrence



Silberstein SD. Neurology 2008

증례

트립탄을 복용하면 두통은 좋아지나 가슴이 조이는 부작용 때문에 불편

해결책:

(1) 다른 트립탄으로 변경: 특히 Naratriptan Almotriptan 또는 Frovatriptan 을 추천

(2) 기존의 트립탄 용량을 줄이고 long acting NSAID(예. Naproxen) 를 추가

편두통이 있을 때마다 트립탄 복용하는데 한 달에 10번 이상 복용함

-- 약물남용두통의 가능성으로 편두통예방치료를 시작한다.

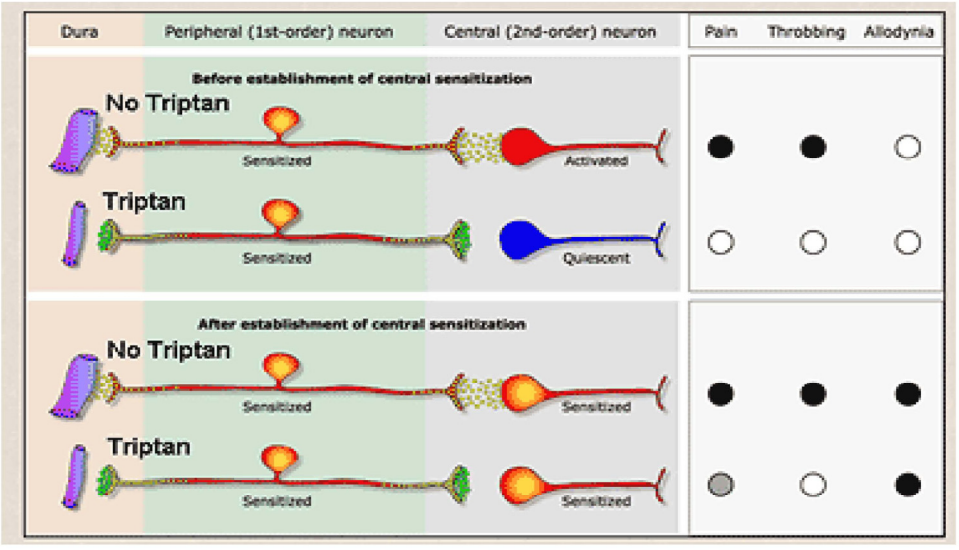
증례

편두통이 생리할 때만 집중적으로 발생

해결책: 미니예방요법
(월경주기가 규칙적인 순수월경무조짐편두통일 경우)
월경시작 또는 두통이 있을 것으로 예상되는 날로부터 2일전부터 3-5일간 복용

(1) *Frovatriptan 2.5 mg or naratriptan 2.5 mg.*
(2) Naproxen 550mg BID

복용시기: 중추감작(central sensitization) 되기 전에 복용해야



FRONTLINE REPORT: HEADACHES

A Hidden Cause of Headache Pain

Pat Sullivan/Associated Press

Painkillers lining the shelves at a drugstore in Houston. A significant number of chronic headaches are caused by overuse of everyday pain medications, experts say.

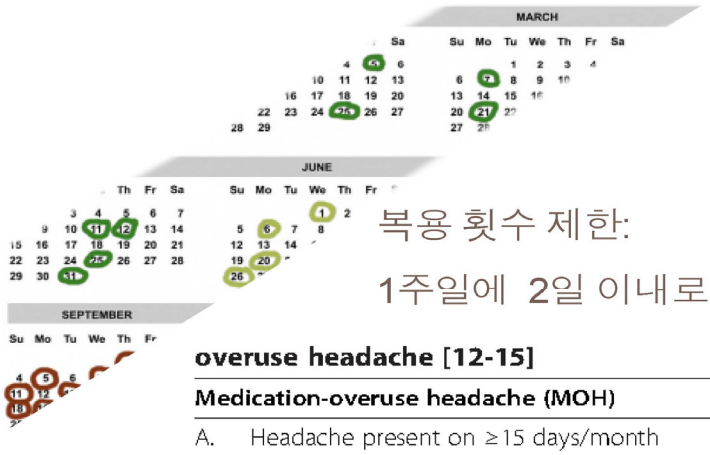
Medication Overuse Headache

Ergotamines OR triptans
≥ 10 days/month on a regular basis ≥ 3 M

Opioids OR combination analgesics
≥ 10 days/month on a regular basis for > 3 M

Simple analgesics
≥ 15 days/month > 3M

Medication overuse headache is avoided
by not using medications for the relief of headache
more than **two or three days a week**.



복용 횟수 제한:

1주일에 2일 이내로 사용하도록 교육

overuse headache [12-15]

Medication-overuse headache (MOH)

A. Headache present on ≥15 days/month

B. Regular overuse for >3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache

C. Headache has developed or markedly worsened during medication overuse

For simple analgesics and for combination of acute medications the intake must be 15 days or more per month, for triptans, ergotamins, opioids and combination analgesics,10 days per month is enough to get the diagnosis of MOH.

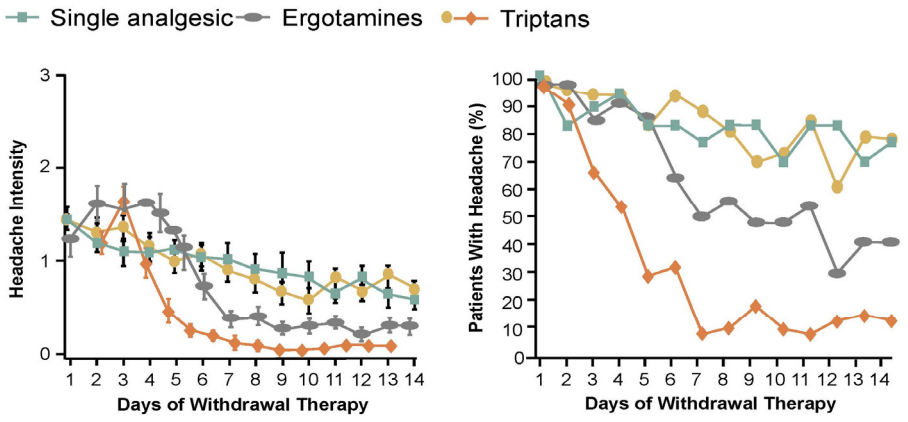
Treatment of Medication Overuse

Education
Life style modification
Trigger avoidance
Exercise
Weight reduction
Sleep care

2. Bridging Tx for 7-10 days

1. Withdrawal: Cold Turkey
3. Prevention : Botulinum toxin, topiramate, topiramate and propranolol

Immediate Decrease in Headache Following Withdrawal of Acute Medications



23 Diener HC, Limmroth V. *Lancet Neurol.* 2004;3:475-483.

Management Approaches for MOH

Overused Treatment	Tapering Strategy	Acute Treatment Options for the Overused Medication[a]	Bridge Therapy[a]
Butalbital combination[b]	Gradual taper	Add a triptan or a nonsteroidal anti-inflammatory drug (NSAID)[c]	Consider a long-acting triptan (eg, naratriptan) Long-acting NSAID (eg, naproxen)[c] Steroid taper (eg, prednisone 60 mg/d for 3 days)[c]
Butalbital combination[b]	Abrupt taper	Substitute phenobarbital and taper Add a triptan or an NSAID[c]	Consider a long-acting triptan Long-acting NSAID if needed
Opioid	Gradual taper	Add a triptan or an NSAID[c]	Consider a long-acting triptan Long-acting NSAID if needed[c]
Triptan/ergot alkaloid	Abrupt or gradual	Add an NSAID[c]	Long-acting NSAID or a steroid taper[c]
NSAID	Abrupt or gradual	Add a triptan	Consider a long-acting triptan

Bridging program for the withdrawal symptoms

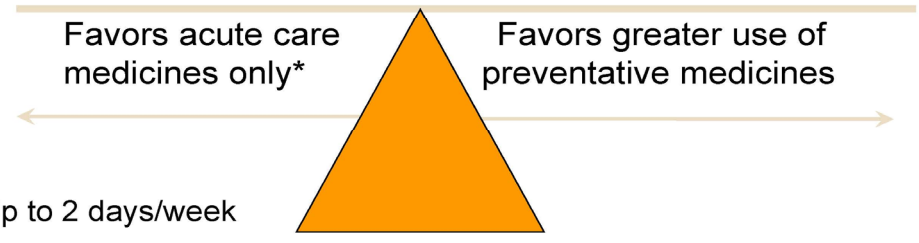
- For 7-10 days
- - Parenteral dihydroergotamine mesylate
  - Long acting NSAIDs (naproxen) for triptan overuser
  - Long acting triptan (frova/naratriptan) for NSAIDs overuser
  - Short course of steroids (dexa 4mg bid or Pd 80mg for 2 days then tapering (-20mg/2d)

Smith TR et al Drug 2004;64:2503-2514

Preventative Migraine Therapy

- Not disabling
- Short duration
- Good response to acute care medications

- Disabling
- Long duration headaches
- Poor response to acute medicines



* Up to 2 days/week

Rapoport AM, Adelman JU. *Am J Managed Care*. 1998:531-544.

Current State of Classification and Diagnosis in CM

ICHD-3 ± Medication Overuse[2] Combined Criteria

- Headache on ≥15 days per month for at least 3 months[1]
- ≥5 prior migraine attacks[1]
- On ≥8 days per month, headache fulfills criteria for migraine[1]
  - ≥2 of the following: a) unilateral b) throbbing c) moderate or severe pain d) aggravated by physical activity
  - ≥1 of the following: a) nausea and/or vomiting b) photophobia and phonophobia
  - Relieved with triptans or ergotamine
- Not attributed to another causative disorder[1]
- Subclassified as with or without medication overuse headache as diagnosed by 8.2[1,2]

Practical Clinical Criteria

Headache ≥15 days /M

&

Current or prior diagnosis of migraine

&

With or without medication overuse

Preventive Treatment in CM

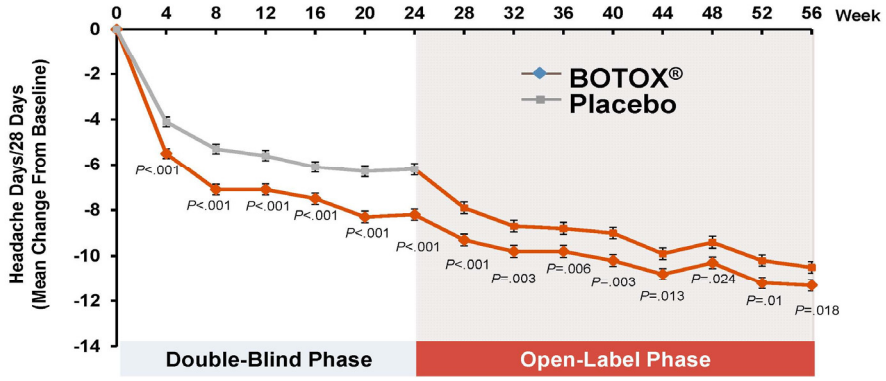
	Chronic Migraine (n=520)	Episodic Migraine (n=9424)
Antiepileptic drugs:		
Divalproex	20%	10%
Topiramate	**33%**	**19%**
Gabapentin	22%	11%
Other	7%	6%
Antidepressants:		
Amitriptyline	**33%**	**17%**
Nortriptyline	9%	5%
Duloxetine	7%	2%
Venlafaxine	7%	5%
Paroxetine	8%	6%
Sertraline	12%	7%
Fluoxetine	11%	6%

	Chronic Migraine (n=520)	Episodic Migraine (n=9424)
Antihypertensives:		
Propranolol	22%	20%
Nadolol	3%	3%
Metoprolol	7%	5%
Atenolol	7%	5%
Verapamil	9%	5%
Diltiazem	0.5%	0.2%
Nutraceuticals/Herbal Therapies:		
Feverfew	10%	12%
Magnesium	11%	10%
Riboflavin	10%	10%
BotulinumToxin		
Occipital Nerve Stimulation		

Data from the American Migraine Prevalence and Prevention (AMPP) study.
Bigal ME et al. *Neurology*. 2008;71;559-566.

Botulinum Toxin A : PREEMPT Study

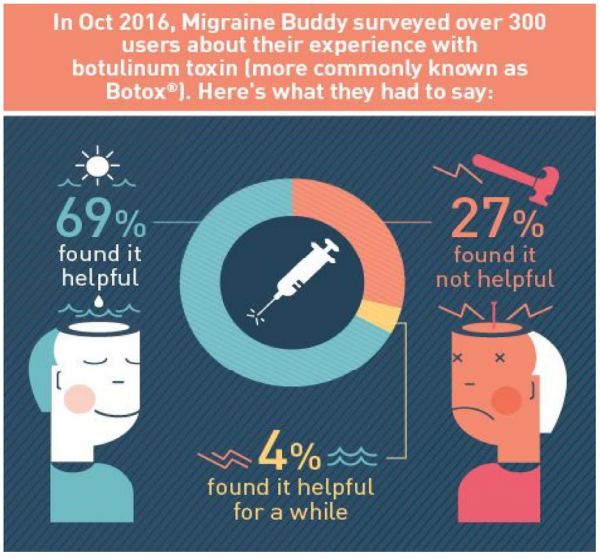
BTX 를 투여 받은 환자에서 편두통 발생일수가 평균적으로 8일 감소
56주 후, BTX 를 투여 받은 환자의 약 70%에서, 편두통 발생일수가 50% 이상 감소

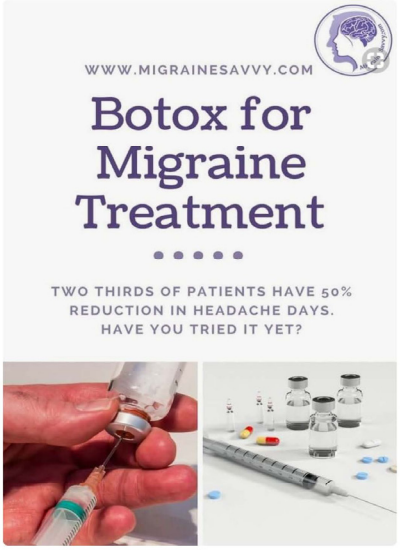


1. Aurora SK, et al. Presented at IHC 2009.

Mean ± standard error.
The double-blind phase included 688 subjects in the BOTOX® group and 696 in the placebo group.
Headache days at baseline: 19.9 BOTOX® group vs 18.9 placebo group, *P*=.328.

Response Rate

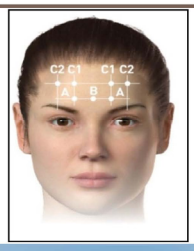




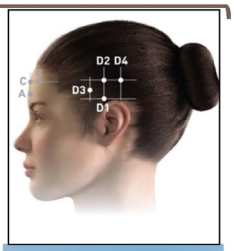
Order of injection and patient position: FSFD

- The anatomic injection sites follow distributions and areas innervated by the trigeminal - cervical nerve complex

Supine

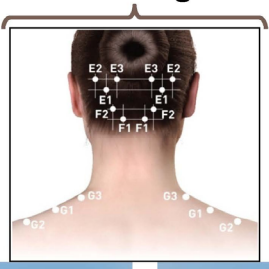


A. Corrugator: 5 U each side
B. Procerus: 5 U (one site)
C. Frontalis: 10 U each side



D. Temporalis: 20 U each side

Sitting



E. Occipitalis: 15 U each side

F. Cervical paraspinal: 10 U each side
G. Trapezius: 15 U each side

0.1 mL = (5 U/site).
Blumenfeld AM et al. Presented at AAN 2010.

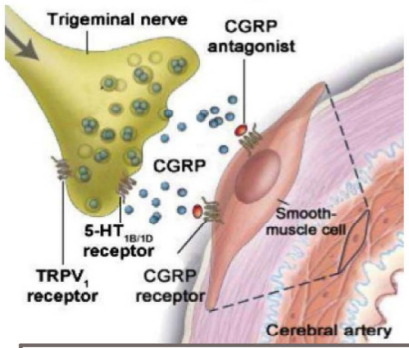
5u x 31 sites=155u

32

Targeting treatment

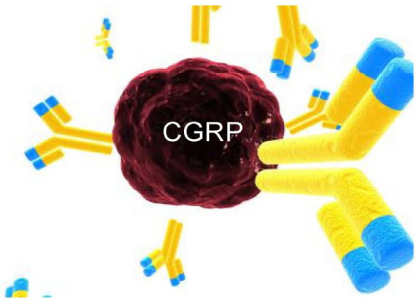
CGRP antagonist vs monoclonal CGRP (-Receptor) Ab

CGRP antagonist



Acute treatment
No vasoconstriction :
Contraindication for triptan
Angina, MI, stroke
Small molecule ; poorly through the BBB

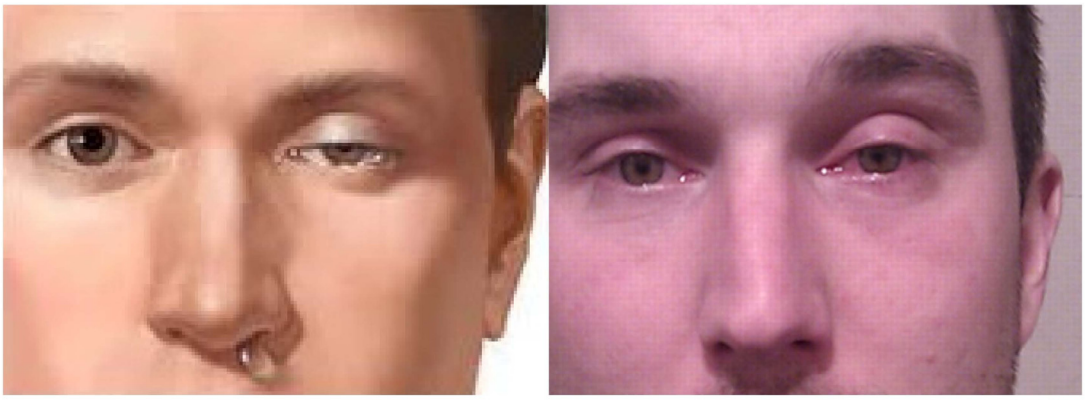
CGRP Ab



Prevention for High freq EM or CM
Larger size, Longer duration
Less possibility to cross the BBB

자율신경증상을 동반하는 두통

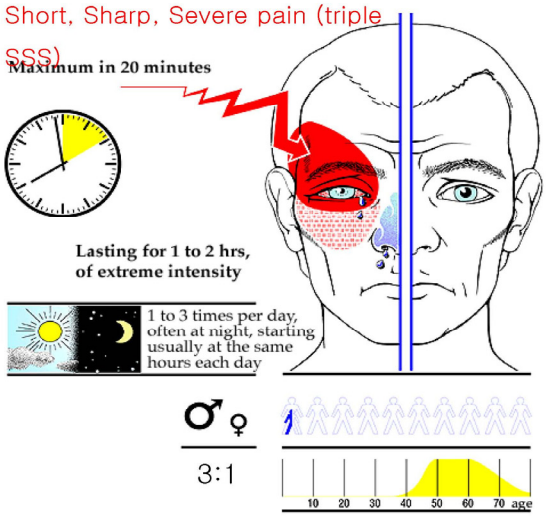
Trigeminal Autonomic Cephalalgias

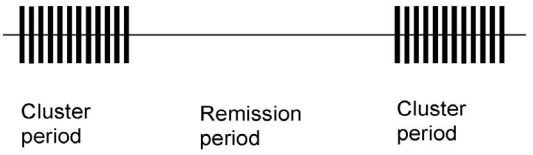


↑Parasympathetic discharge (conjunctival tearing, rhinorrhea)

↓Sympathetic paresis (Miosis, Horner's)

Clinical Pearls on Diagnosing CH

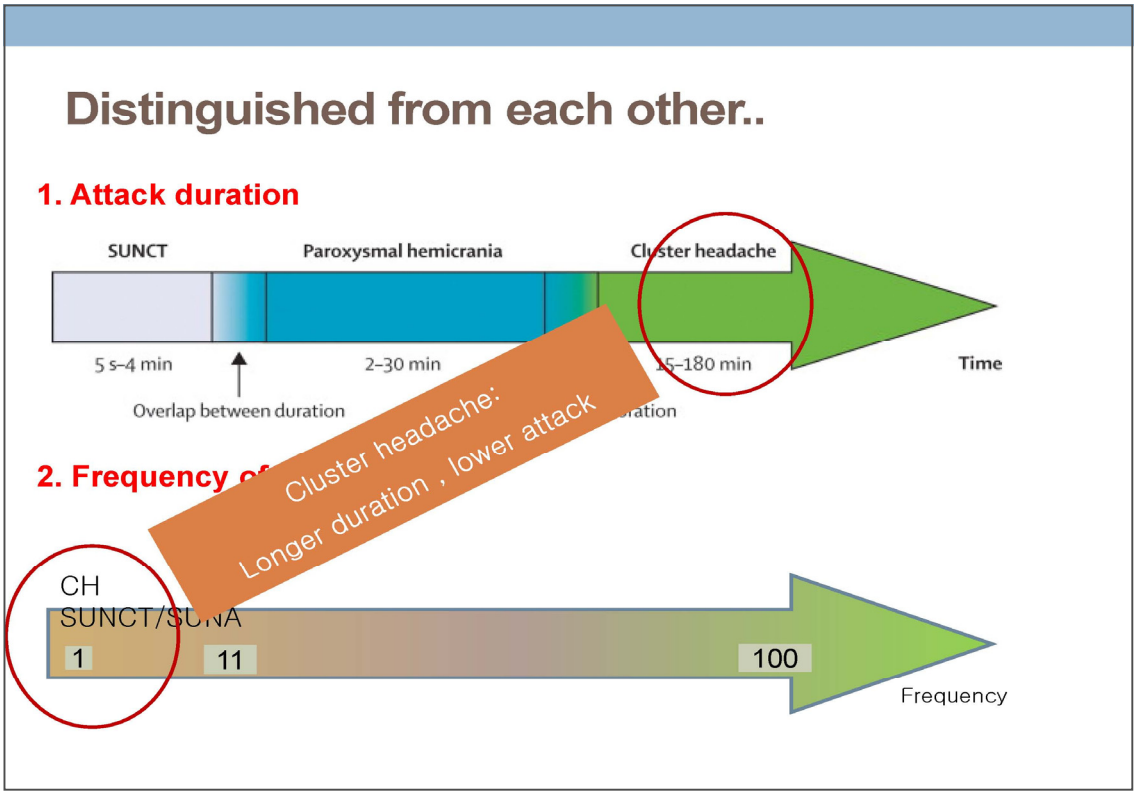


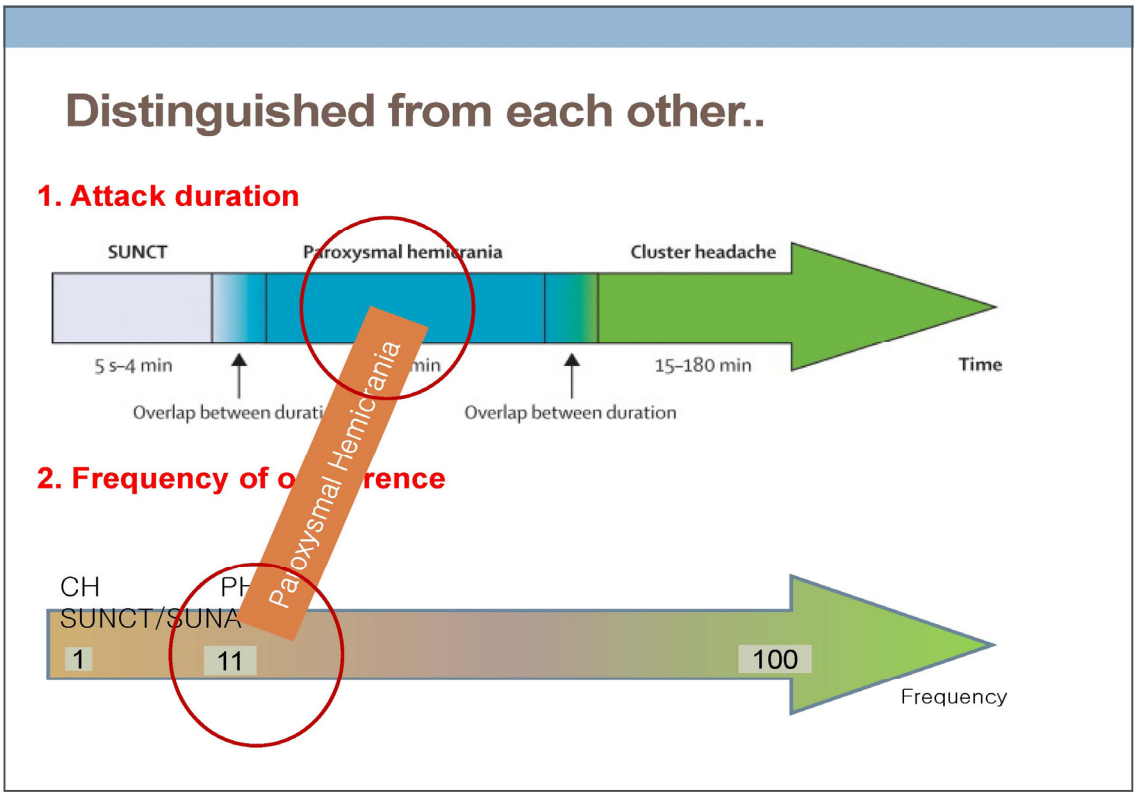


- > 1 month: episodic
- < 1 month: chronic (10%-15%)
- 27% of patients: only a single cluster period

Clinical Pearls on Diagnosing cluster headache

- Short, Sharp, and Severe attacks (triple SSS)
- Parasympathetic activation + Sympathetic paresis + Agitation
- Alarm clock periodicity
- Cluster patients in cycle rarely, if ever, drink alcohol, due to the severity of the trigger
- Smoking is common in cluster patients
- In about one-third of there can be low level ipsilateral interictal pain


Distinguished from each other..
1. Attack duration
SUNCT
Paroxysmal hemicrania
Cluster headache
5 s–4 min
2–30 min
15–180 min
Time
Overlap between duration
Cluster headache:
Longer duration , lower attack
2. Frequency of
CH
SUNCT/SUNA
1
11
100
Frequency


Distinguished from each other..
1. Attack duration
SUNCT
Paroxysmal hemicrania
Cluster headache
5 s–4 min
15–180 min
Time
Overlap between duration
Overlap between duration
2. Frequency of occurrence
Paroxysmal Hemicrania
CH
SUNCT/SUNA
1
11
100
Frequency

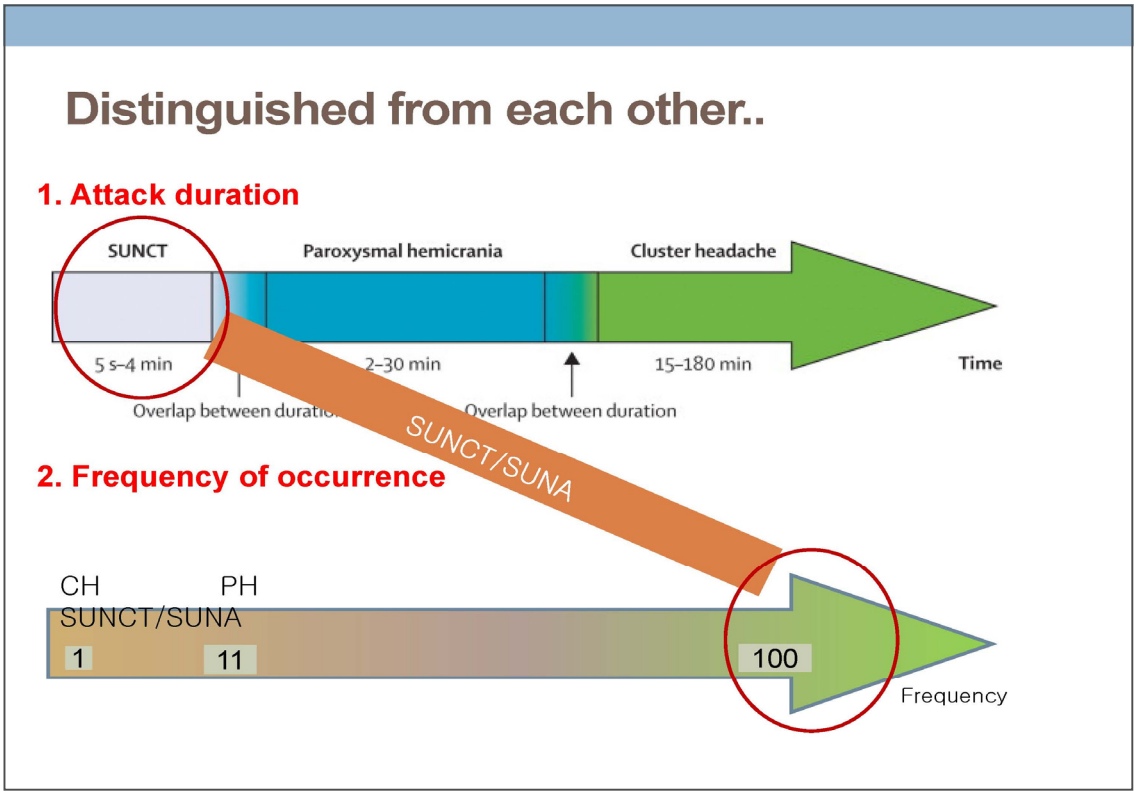


Table 2.12 Differential points among the TACs

Features	Cluster headache	Paroxysmal hemicrania	SUNCT/SUNA
Gender (M/F)	3–6/1	1/1	1.5/1
Pain quality	Stab/sharp/throb/poker	Stab/sharp/throb/poker	Stab/sharp/throb/poker
Severity	Very severe	Severe – very severe	severe
Distribution	$V_1 > C2 > V_2 > V_3$	$V_1 > C2 > V_2 > V_3$	$V_1 > C2 > V_2 > V_3$
Attack frequency	Every other day–8/day	Mean 11; up to 30/day	Mean 100; >100/day
Length	15–180 min	2–30 min	4–240 s
Migraine features			
Nausea	50%	40%	25%
Photo-/phonophobia	65%	65%	25%
Triggers			
Alcohol	Yes	Yes	No
Nitroglycerin	Yes	Yes	No
Cutaneous triggers	No	No	Yes
Agitation/restlessness	90%	80%	65%
Episodic/chronic	9/1	1/2	1/9
Circadian/circannual periodicity	Yes	No	No
Treatment efficacy			
Oxygen	70%	None	None
Sumatriptan subcutaneously	90%	20%	10% or less
Indomethacin	None	100%	None

유발되는 두통

Headache Classification and contents

Part 1
The primary headaches

Part 2
The secondary headaches

Part 3
Cranial neuralgias other facial pain and other headaches

Appendix

1. Migraine
2. Tension-type headache
3. Trigeminal autonomic cephalalgia
4. **Other primary headache**

Four subgroups in other primary headache

Physical exertion	• 4.1 Primary cough headache • 4.2 Primary exercise headache • 4.3 Primary headache associated with sexual activity • 4.4 Primary thunderclap headache
Direct physical stimuli	• 4.5 Cold-stimulus headache • 4.6 External-pressure headache
Epicranial (scalp) headaches	• 4.7 Primary stabbing headache • 4.8 Nummular headache
Others	• 4.9 Hypnic headache • 4.10 New daily persistent headache (NDPH)

- **50세 남자**가 갑자기 발생한 두통을 주소로 내원하였다. 터질 것 같은 심한 두통이 **기침을 하는 중에 발생**하여 **약 30분간 지속**하였다. 그 후 주로 기침할 때 비슷한 양상의 두통이 반복되었고 무기운 물건을 들 때와 대변을 보던 중에도 한차례씩 발생하였다. 뇌척수액검사에서 출혈은 관찰되지 않았고 뇌영상은 정상소견이었다. 2년 정도 지속되다가 호전되었다.

Diagnostic criteria: ICHD3

A. At least two headache episodes

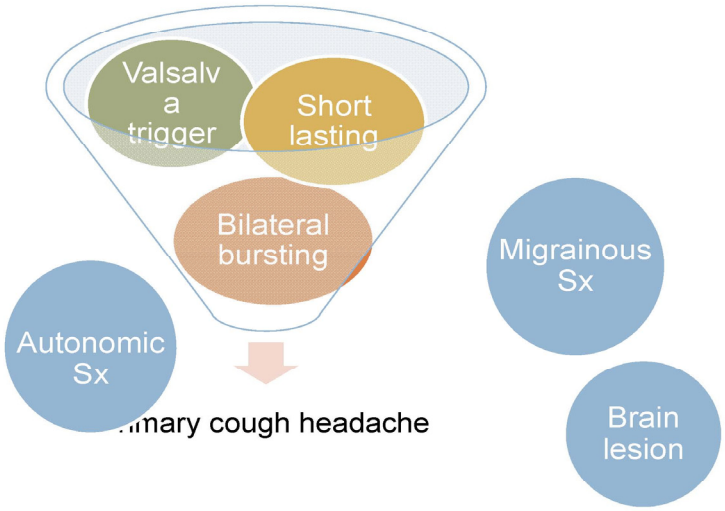
B. Brought on by and occurring only in association with coughing, straining and/or other Valsalva maneuver

C. Sudden onset

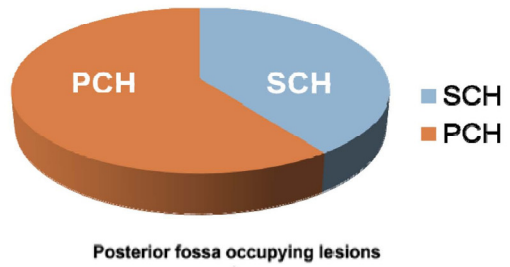
D. Lasting between 1 second and 2 hours

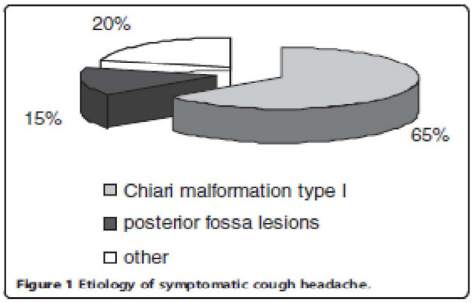
E. Not better accounted for by another ICHD-3 diagnosis.

Major Characteristics of PCH



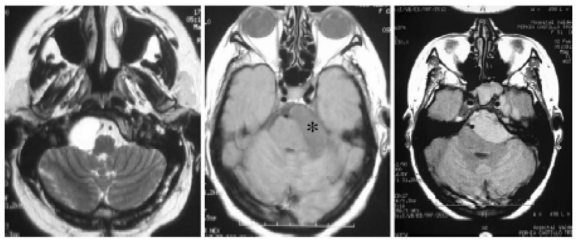
Symptomatic Cough Headache

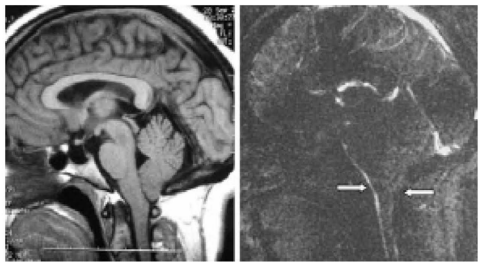




Posterior fossa occupying lesions

3 arachnoid cysts | 2 dermoid tumors | 2 meningiomas



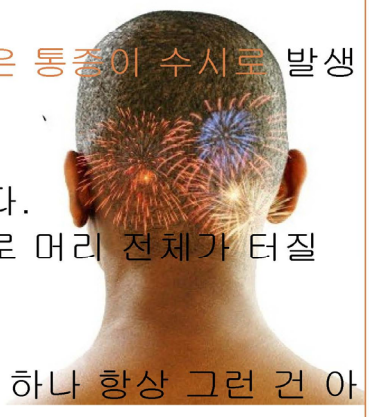


Diagnostic workup

MRI	• Should be done • For posterior fossa lesions
with Gd	• Should be done • For spontaneous CSF leak
MRA	• Seems reasonable to obtain • For an unruptured aneurysm
Carotid US	• Not typically do

CASE

- 58세 남자
- 순간적으로 우측 뒷목이 찢어질 것 같은 통증이 수시로 발생함. 하루에도 수 차례.
- 전기에 감전된 듯 찌릿한 통증.
- 통증이 양쪽 뒷목에서 시작될 때도 있다.
- 심할 때는 양쪽 눈까지 퍼지는 양상으로 머리 전체가 터질 듯하다.
- 목 디스크가 심해지지는 않았다고 함.
- ***뒷목을 누르면 상기 통증이 유발***되기도 하나 항상 그런 건 아니다.
- 대상포진 초기 의심된다며 약을 처방 받았으나 효과 없었음.



Case 비교

- 45세 여자가 2일전부터 우측 후두부의 통증을 주소로 내원하였다. 통증은 갑자기 아주 짧은 시간 콱 찌르는 양상으로 나타났는데 2-3분에 한번씩 반복하였다. 통증이 오면 깜짝 놀래서 환자는 자기도 모르게 손을 찌르는 부위에 갖다 대었다. 두통의 과거력은 없었으며 최근 회사일로 많이 피곤하였다. 환자의 통증은 소염진통제 투여 후 4일째 증상이 소실되었다.

4.7 Primary stabbing headache

ICHD3 beta

A. Head pain occurring spontaneously as a single stab or series of stabs and fulfilling criteria B–D

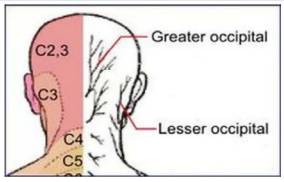
B. Each stab lasts for up to a few seconds

C. Stabs recur with irregular frequency, from one to many per day

D. No cranial autonomic symptoms

E. Not better accounted

DIAGNOSTIC CRITERIA OF OCCIPITAL NEURALGIA



A. Unilateral or bilateral pain fulfilling criteria B-E

B. Pain is located in the distribution of the greater, lesser and/or third occipital nerves

C. Pain has two of the following three characteristics:

1. recurring in paroxysmal attacks lasting from a few seconds to minutes
2. severe intensity
3. shooting, stabbing or sharp in quality

D. Pain is associated with both of the following:

1. dysaesthesia and/or allodynia apparent during innocuous stimulation of the scalp and/or hair
2. either or both of the following:
   a) tenderness over the affected nerve branches
   b) trigger points at the emergence of the greater occipital nerve or in the area of distribution of C2

E. Pain is eased temporarily by local anaesthetic block of the affected nerve

F. Not better accounted for by another ICHD-3 diagnosis.

Main take-away points

1. Primary headache vs secondary headache
2. Red flags sign: SNOOP4
3. Thunderclap headache

   --Many other serious causes of a “thunderclap” headache besides SAH

   -- Do the LP after negative CT if suspect SAH
4. We should not miss secondary, pathological headache.

   We cannot neglect primary headache.