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Headaches Not to Miss and Red Flags

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Learning Objectives

Upon completion of this activity, learners will be able to:

- Recognize red flags when assessing headache presentations
- Identify key clinical features and characteristics of some common & serious secondary headaches
- Appropriately use imaging techniques for relevant secondary headache disorders

This presentation does not cover an exhaustive list of secondary headaches
We will cover some serious headaches in the categories of:

- Vascular disorders
- Intracranial pressure disorders

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Red Flags for secondary Headache: “SNOOP”

S	Systemic signs or symptoms	Fever, weight loss, malignancy, HIV, meningismus, pregnancy
N	Neurologic signs or symptoms	Papilledema, hemiparesis, hemi-sensory loss, diplopia, dysarthria
O	Onset	“Worst headache of life” (thunderclap)
O	Older	New headache at age ≥50
P	Progression of existing headache disorder, positional	Change in quality, frequency, or location, or major change with position, or precipitated by valsalva

Dodick DW. *Adv Stud Med* 2003;3:S550-S555.

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SNNOOP10

Sign or symptom	Related secondary headaches	Flag Colour
Systemic symptoms including fever	Headache attributed to infection or nonvascular intracranial disorders, carcinoid or pheochromocytoma	Red (orange for isolated fever)
Neoplasm in history	Neoplasms of the brain; metastasis	Red
Neurologic deficit or dysfunction (including decreased consciousness)	Headaches attributed to vascular, nonvascular intracranial disorders; brain abscess and other infections	Red
Onset of headache is sudden or abrupt	Subarachnoid hemorrhage and other headaches attributed to cranial or cervical vascular disorders	Red
Older age (after 50 years)	Giant cell arteritis, other headache attributed to cranial or cervical vascular disorders; neoplasms and other nonvascular intracranial disorders	Red

Do, T.P., et al., Red and orange flags for secondary headaches in clinical practice: SNNOOP10 list. Neurology, 2019. 92(3): p. 134-144.

Sign or symptom	Related secondary headaches	Flag Colour
Pattern change or recent onset of headache	Neoplasms, headaches attributed to vascular, nonvascular intracranial disorders	Red
Positional headache	Intracranial hypertension or hypotension	Red
Precipitated by sneezing, coughing, or exercise	Posterior fossa malformations; Chiari malformation	Red
Papilledema	Neoplasms and other nonvascular intracranial disorders; intracranial hypertension	Red
Progressive headache and atypical presentations	Neoplasms and other nonvascular intracranial disorders	Red

Do, T.P., et al., Red and orange flags for secondary headaches in clinical practice: SNNOOP10 list. Neurology, 2019. 92(3): p. 134-144.

Sign or symptom	Related secondary headaches	Flag Colour
Pregnancy or puerperium	Headaches attributed to cranial or cervical vascular disorders; postdural puncture headaches; hypertension-related disorders (e.g., preeclampsia); cerebral sinus thrombosis; hypothyroidism; anemia; diabetes	Red
Painful eye with autonomic features	Pathology in posterior fossa, pituitary region, or cavernous sinus; Tolosa-Hunt syndrome; ophthalmic causes	Red
Post-traumatic onset of headache	Acute and chronic post-traumatic headache; subdural hematoma and other headache attributed to vascular disorders	Red
Pathology of the immune system such as HIV	Opportunistic infections	Red
Painkiller overuse or new drug at onset of headache	Medication overuse headache; drug incompatibility	Red

Do, T.P., et al., Red and orange flags for secondary headaches in clinical practice: SNNOOP10 list. Neurology, 2019. 92(3): p. 134-144.

Vascular Disorders

Thunderclap Headache

- A severe headache which comes on very abruptly and reaches maximal intensity in less than one minute
- Like a “clap of thunder”

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Differential Diagnosis of Thunderclap headache

Primary:

- Primary thunderclap headache
- Primary exertional, cough, or sexual headaches
- Migraine

Secondary:

Vascular:

- SAH
- Sentinel headache
- Intracranial hemorrhage
- Retroclival hematoma
- RCVS
- Cerebral Venous sinus thrombosis
- Dissection (cervical or vertebral)
- Pituitary apoplexy
- Ischemic stroke
- Hypertensive emergency, PRES

Non-vascular

- Intracranial infection (meningitis)
- Colloid cyst of 3rd ventricle
- Spontaneous intracranial hypotension

Kopel D, Peeler C, Zhu S. Headache Emergencies. Neurol Clin. 2021 May;39(2):355-372.

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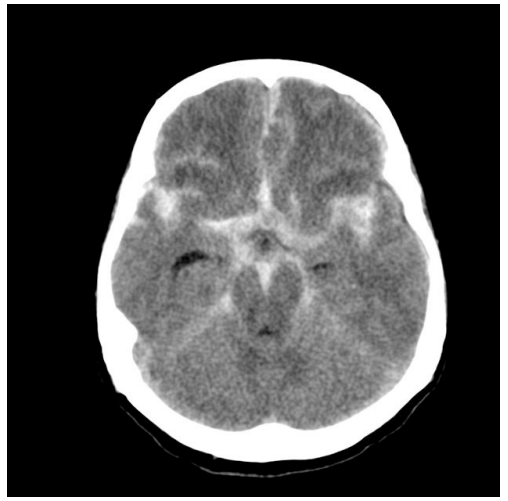
Typical ER workup of thunderclap headache

- CT head
  - 98% specificity, near 100% sensitivity for SAH during first 12 hrs after h/a onset
- If CT head negative, then Lumbar puncture
  - Cell count, protein, glucose, xanthochromia, OP
  - Spectrophotometry (analysis for bilirubin) near 100% sensitive when LP done at 12 hrs to 2 weeks
  - If LP not possible, then CTA often performed
- If CT and LP negative, then MRI with MRA/MRV or CTA/CTV as soon as possible

Kopel D, Peeler C, Zhu S. Headache Emergencies. Neurol Clin. 2021 May;39(2):355-372.

Subarachnoid hemorrhage (SAH)

- Headache can be the sole symptom of non-traumatic SAH
- Mortality 40-50%; 10-20% of patients die before reaching hospital
- 50% of survivors remain disabled



Radiopaedia.org

ICHD-3 Diagnostic criteria:

A. Any new headache fulfilling criteria C and D

B. Subarachnoid haemorrhage (SAH) in the absence of head trauma has been diagnosed

C. Evidence of causation demonstrated by at least two of the following:
   1. headache has developed in close temporal relation to other symptoms and/or clinical signs of SAH, or has led to the diagnosis of SAH
   2. headache has significantly improved in parallel with stabilization or improvement of other symptoms or clinical or radiological signs of SAH
   3. headache has sudden or thunderclap onset

D. Either of the following:
   1. headache has resolved within 3 months
   2. headache has not yet resolved but 3 months have not yet passed

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

Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018 Jan;38(1):1-211.

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Reversible Cerebral Vasoconstriction Syndrome

A syndrome characterized by:

- Severe thunderclap headaches with or without focal neurological deficits
- Diffuse segmental constriction of cerebral arteries
- Spontaneous resolution within 3 months

- Failure of regulation of arterial tone & sympathetic overactivity
- Headache can be triggered by sexual activity, valsalva, stress, bathing, swimming, etc.
- Many precipitants have also been described, such as vasoactive drugs, postpartum period, etc.
- Headache is main symptom and often only symptom
- Often recurs in the first 1-3 weeks (mean of 4 attacks)
- Some patients can develop transient or persistent focal neurological deficits and a few can have seizures

- Hemorrhagic complications can occur early (usually first week), are more common in women and in patients with a prior history of migraine

- Infarctions occur later (2nd week) and occur mainly in arterial watershed regions

Singhal AB. Reversible cerebral vasoconstriction syndrome: A review of pathogenesis, clinical presentation, and treatment. Int J Stroke. 2023 Dec;18(10):1151-1160.

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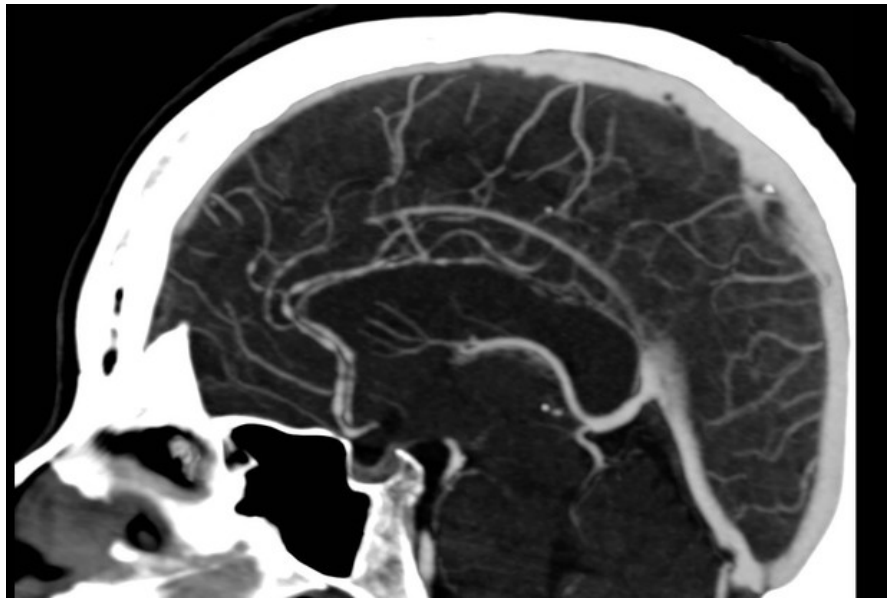
Neuroimaging in RCVS

- MRI brain is often normal, but can show:
- Convexity subarachnoid hemorrhage
  - Non-aneursymal, often mild
- Intracerebral hemorrhage
  - Usually single and lobar
- Cerebral infarction
  - Watershed regions
- Reversible brain edema
  - Frequently associated with stroke or hemorrhage
  - Resolves much earlier than vasoconstriction
- Direct or indirect (CTA or MRA) angiography required to show segmental narrowing and dilatation of cerebral arteries
- “string of beads” appearance



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Singhal AB. Reversible cerebral vasoconstriction syndrome: A review of pathogenesis, clinical presentation, and treatment. Int J Stroke. 2023 Dec;18(10):1151-1160.

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RCVS - ICHD-3 criteria

A. Any new headache fulfilling criterion C

B. Reversible cerebral vasoconstriction syndrome (RCVS) has been diagnosed

C. Evidence of causation demonstrated by at least one of the following:

1. headache, with or without focal deficits and/or seizures, has led to angiography (with 'strings and beads' appearance) and diagnosis of RCVS
2. headache has one or more of the following characteristics:
   a) thunderclap onset
   b) triggered by sexual activity, exertion, Valsalva manœuvres, emotion, bathing and/or showering
   c) Present or recurrent during ≤1 month after onset, with no new significant headache after >1 month

D. Either of the following:

1. headache has resolved within 3 months of onset
2. headache has not yet resolved but 3 months from onset have not yet passed

E. Not better accounted for by another ICHD-3 diagnosis, and aneurysmal subarachnoid haemorrhage has been excluded by appropriate investigations.

Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018 Jan;38(1):1-211.

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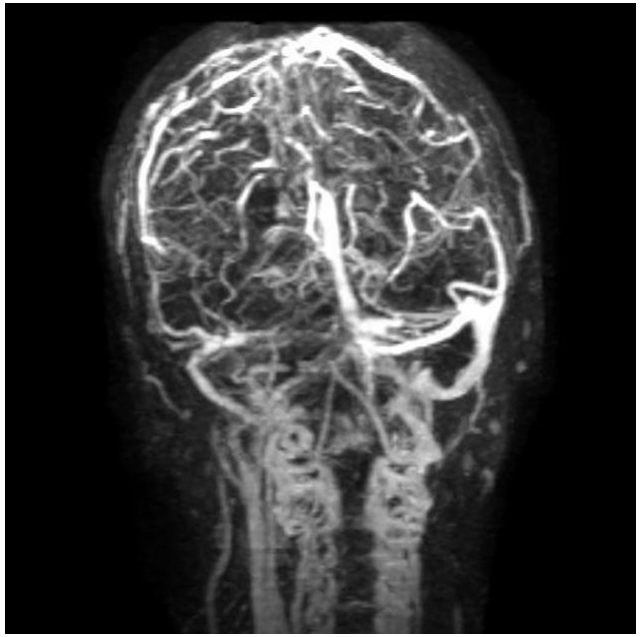
Cerebral Venous Sinus Thrombosis

- Keep this diagnosis in mind for any patient presenting with:
  - symptoms/signs of increased intracranial pressure
  - Having risk factors for venous thrombosis, including use of OCP/hormonal therapies, prothrombotic states, etc.
  - Headache can present as thunderclap, but more often acute or subacute
  - Diagnosis is based on neuroimaging (MRI/MRV or CTV and intra-arterial angiography in doubtful cases)



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- Ropper AH, Klein JP. Cerebral Venous Thrombosis. N Engl J Med. 2021 Jul 1;385(1):59-64.

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CVST – ICHD-3 criteria

A. Any new headache, fulfilling criterion C

B. Cerebral venous thrombosis (CVT) has been diagnosed

C. Evidence of causation demonstrated by both of the following:
   1. headache has developed in close temporal relation to other symptoms and/or clinical signs of CVT, or has led to the discovery of CVT
   2. either or both of the following:
      a) headache has significantly worsened in parallel with clinical or radiological signs of extension of the CVT
      b) headache has significantly improved or resolved after improvement of the CVT

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

Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018 Jan;38(1):1-211.

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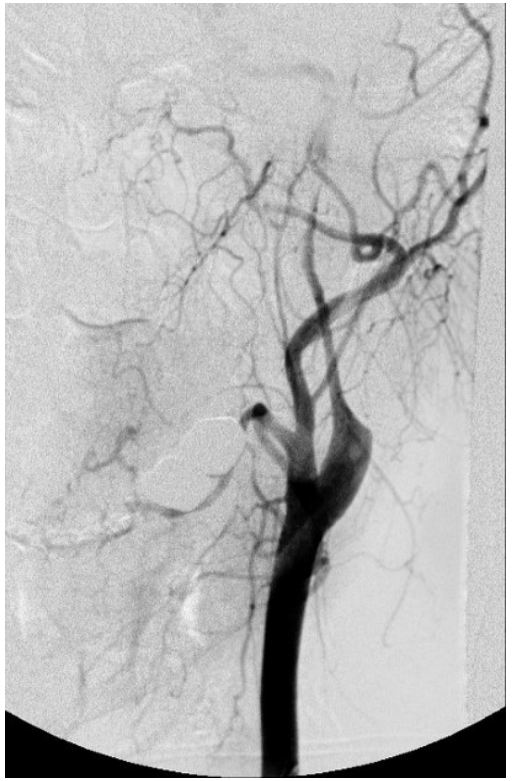
Cervical Carotid or Vertebral Artery Dissection

- Headache, facial pain and/or neck pain caused by dissection of a cervical carotid or vertebral artery
- Diagnosed by angiography (CTA, MRA or cerebral angio if needed)
- The pain is usually ipsilateral to the dissected vessel
- Generally sudden/thunderclap onset, but not always
- It can remain isolated or be a warning symptom preceding ischaemic stroke
- Associated signs and symptoms can occur, such as Horner's syndrome



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Yaghi S, et al. Treatment and Outcomes of Cervical Artery Dissection in Adults: A Scientific Statement From the American Heart Association. Stroke. 2024 Mar;55(3):e91-e106.

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Cervical Carotid or Vertebral artery Dissection ICHD-3 criteria

A. Any new headache and/or facial or neck pain fulfilling criteria C and D

B. Cervical carotid or vertebral dissection has been diagnosed

C. Evidence of causation demonstrated by at least two of the following:
   1. pain has developed in close temporal relation to other local signs of the cervical artery dissection, or has led to its diagnosis
   2. either or both of the following:
      a) pain has significantly worsened in parallel with other signs of the cervical artery dissection
      b) pain has significantly improved or resolved within 1 month of its onset
   3. either or both of the following:
      a) pain is severe and continuous for days or longer
      b) pain precedes signs of acute retinal and/or cerebral ischaemia
   4. pain is unilateral and ipsilateral to the affected cervical artery

D. Either of the following:
   1. headache has resolved within 3 months
   2. headache has not yet resolved but 3 months have not yet passed

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

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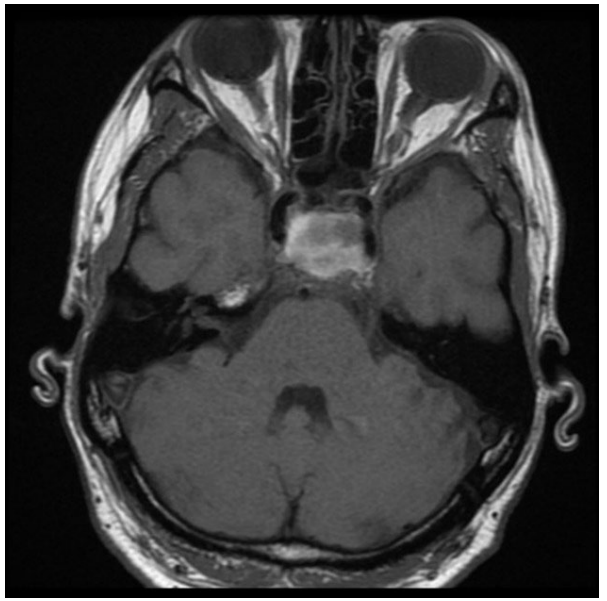
Pituitary Apoplexy

- Acute, often life-threatening condition
- Most cases occur as first presentation of rapid enlargement of non-functioning pituitary macroadenomas due to hemorrhage and/or infarction
- Important to think about during pregnancy and postpartum
- CT is often completed in ER settings but MRI sella provides more detail
- Headache presentation is usually sudden/thunderclap and severe
- Often accompanied by visual deficits such as temporal VF defects
- There may also be signs of hypopituitarism



Radiopaedia.org

Iglesias P. Pituitary Apoplexy: An Updated Review. J Clin Med. 2024 Apr 24;13(9):2508.

Pituitary Apoplexy – ICHD-3 criteria

A. Any new headache fulfilling criterion C
B. Acute haemorrhagic pituitary infarction has been diagnosed
C. Evidence of causation demonstrated by at least two of the following:
    1. headache has developed in close temporal relation to other symptoms and/or clinical signs of pituitary apoplexy, or has led to the diagnosis of pituitary apoplexy
    2. either or both of the following:
        a) headache has significantly worsened in parallel with other symptoms and/or clinical signs of pituitary apoplexy
        b) headache has significantly improved in parallel with other symptoms and/or clinical signs of improvement of pituitary apoplexy
    3. headache is severe and of sudden or thunderclap onset
D. Not better accounted for by another ICHD-3 diagnosis.

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Intracranial Pressure Disorders

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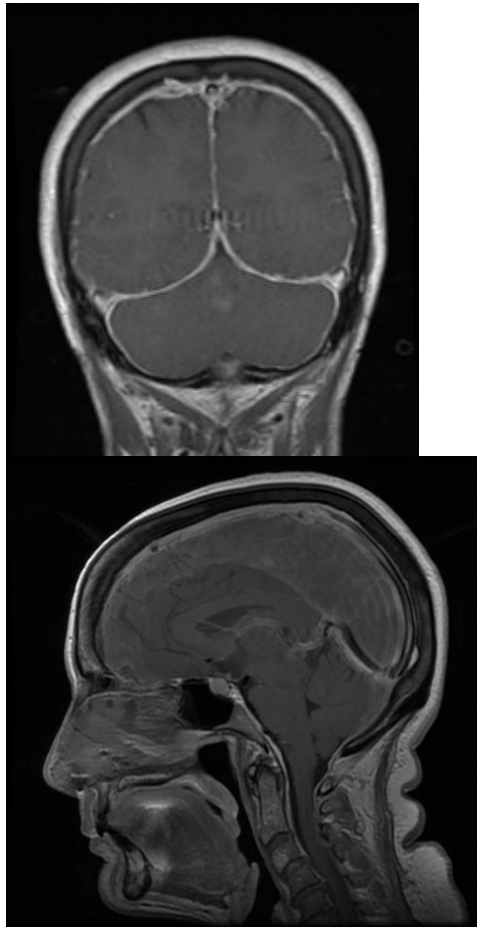
Spontaneous Intracranial Hypotension

- SIH is caused by spontaneous spinal CSF leaks
- Classic presentation is subacute orthostatic headache, but can also present as thunderclap or acute onset
- May be associated with many other neurological symptoms, such as muffled hearing, imbalance, nausea, cognitive dysfunction, etc.
- Often causes significant disability
- Untreated spinal CSF leaks can cause long-term complications, such as bibrachial amyotrophy, superficial siderosis, frontotemporal brain sagging
- MRI brain enhanced and heavily T2 weighted MR spine (non-invasive myelogram) assist with diagnosis
- Leak localization by CT or digital subtraction myelography



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ICHD-3 Diagnostic Criteria for Low CSF Pressure

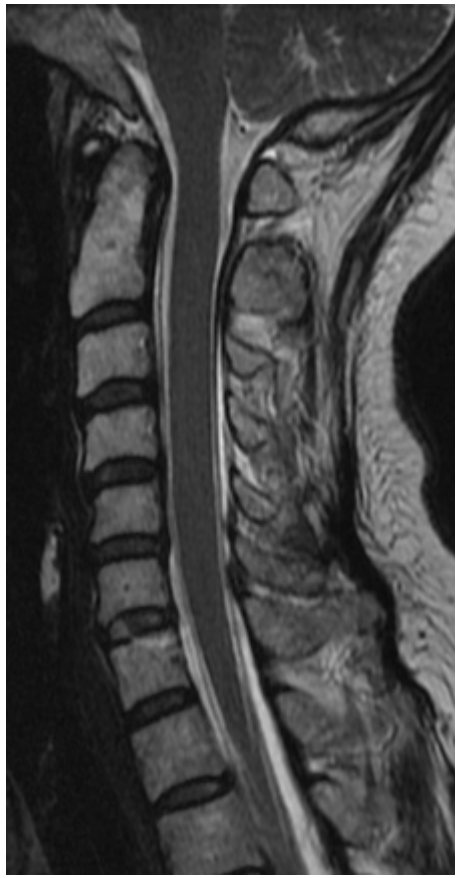
A. Any headache fulfilling criterion C

B. Either or both of the following:
   1. Low CSF pressure (<60 mm CSF)
   2. Evidence of CSF leakage on imaging

C. Headache has developed in temporal relation to the low CSF pressure or CSF leakage, or has led to its discovery

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

*In addition, Criteria of: “Absence of a procedure or trauma known to be able to cause CSF leakage” required for SIH



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Differential Diagnosis of Intracranial Hypertension

- Mass lesion (including choroid plexus papilloma)
- Adhesions of arachnoid granulations (e.g. from SAH or meningitis)
- Obstructive hydrocephalus (e.g. aqueductal stenosis)
- Intracranial venous sinus obstruction:
  - Venous sinus thrombosis
  - Neck surgery
  - Jugular venous compression

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Differential diagnosis of Intracranial Hypertension

Endocrine

- Hyperaldosteronism
- Hypoparathyroidism
- Hypothyroidism
- Cushings disease
- Addisons

Systemic

- Nephrotic syndrome
- SLE, GBS,
- APLA syndrome
- Bechet's
- Hypercapnia (OSA)

Drugs

- GH, cyclines, nalidixic acid, sulfa drugs, anabolic steroids, lithium, steroid withdrawal, vitamin A and retinoids

- Friedman DI. The Pseudotumor Cerebri Syndrome. Neurol Clin. 2024 May;42(2):433-471.
- Guarnizo A, Albreiki D, Cruz JP, Létourneau-Guillon L, Iancu D, Torres C. Papilledema: A Review of the Pathophysiology, Imaging Findings, and Mimics. Can Assoc Radiol J. 2022 Aug;73(3):557-567.

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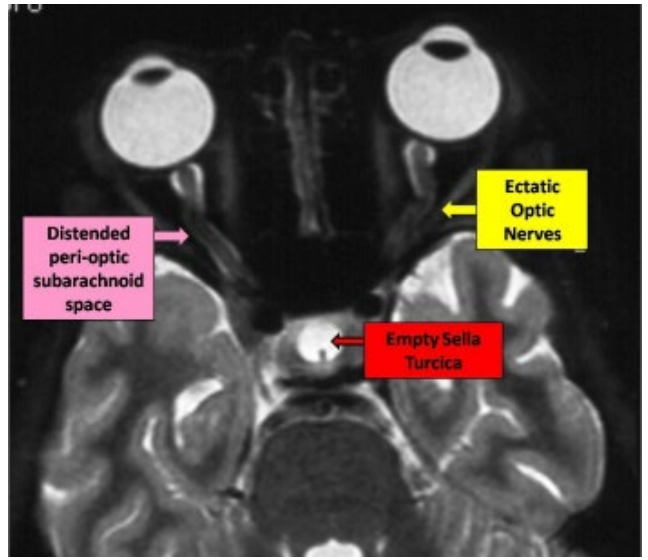
Idiopathic Intracranial Hypertension

- Most often seen in obese women during childbearing years
- Most common symptom is headache present in over 90% of patients
  - Usually bilateral, holocephalic
  - Can be worse supine or in am
- Transient visual obscurations
- Pulsatile tinnitus
- Diplopia and Visual field deficits
- Visual loss to various extents occurs in about 1/3 of pts
- Fulminant IIH: severe visual loss within 4 weeks from symptoms onset
- All patients should be assessed by Neuro-ophthalmology and have VF tests and OCT
- All patients need neuroimaging with MRI
- Venous imaging such as CTV and MRV must also be done to exclude venous thrombosis
- Main goal is to preserve vision, then to reduce headache



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Idiopathic Intracranial Hypertension
ICHD-3 Diagnostic Criteria

A. New headache, or a significant worsening of a pre-existing headache, fulfilling criterion C

B. Both of the following:
   1. idiopathic intracranial hypertension (IIH) has been diagnosed
   2. cerebrospinal fluid (CSF) pressure exceeds 250 mm CSF (or 280 mm CSF in obese children)

C. Either or both of the following:
   1. headache has developed or significantly worsened in temporal relation to the IIH, or led to its discovery
   2. headache is accompanied by either or both of the following:
      a) pulsatile tinnitus
      b) papilloedema

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

*NB: Cerebral venous thrombosis must be ruled out with appropriate imaging.

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New Onset Headache in the Elderly

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Differential Diagnosis of New Onset Headache in the Elderly

Primary Headaches:

- Hypnic headache
- Typical aura without headache
- SUNCT & SUNA
- Primary cough headache
- Tension headaches

Secondary Headaches:

- Mass lesion
- Giant Cell Arteritis (GCA)
- Ischemic or hemorrhagic stroke
- Post-traumatic headaches
- Cardiac cephalalgia (ACS)
- Secondary to medications
  - nitrates, sedatives, stimulants, levodopa, anti-hypertensives, bronchodilators, chemo agents, hormones, erectogenic agents, etc.
- Acute 1° angle-closure glaucoma
- Metabolic
  - hypothyroidism, COPD, anemia, OSA, dialysis, etc.

Stern, JI et al. Headache in Older adults. Practical Neurology May/June 2023. pp 46-50.

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2022 American College of Rheumatology (ACR)/EULAR classification criteria for giant cell arteritis (GCA)

CLASSIFICATION CRITERIA FOR **GIANT CELL ARTERITIS**

CONSIDERATIONS WHEN APPLYING THESE CRITERIA

- **These classification criteria should be applied to classify the patient as having giant cell arteritis when a diagnosis of medium-vessel or large-vessel vasculitis has been made**
- **Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria**

ABSOLUTE REQUIREMENT

Age ≥ 50 years at time of diagnosis	

ADDITIONAL CLINICAL CRITERIA

Morning stiffness in shoulders/neck	+2
Sudden visual loss	+3
Jaw or tongue claudication	+2
New temporal headache	+2
Scalp tenderness	+2
Abnormal examination of the temporal artery[1]	+2

LABORATORY, IMAGING, AND BIOPSY CRITERIA

Maximum ESR ≥ 50 mm/hour or maximum CRP ≥ 10 mg/liter[2]	+3
Positive temporal artery biopsy or halo sign on temporal artery ultrasound[3]	+5
Bilateral axillary involvement[4]	+2
FDG-PET activity throughout aorta[5]	+2

Sum the scores for 10 items, if present. A score of ≥ 6 points is needed for the classification of GIANT CELL ARTERITIS.

DCVAS Study Group, Ponte, C., et al. (2022). 2022 American College of Rheumatology/EULAR Classification Criteria for Giant Cell Arteritis. Arthritis and Rheumatology, 74(12), 1881-1889.

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ICHD-3 Diagnostic Criteria

A. Any new headache fulfilling criterion C
B. Giant cell arteritis (GCA) has been diagnosed
C. Evidence of causation demonstrated by at least two of the following:
    1. headache has developed in close temporal relation to other symptoms and/or clinical or biological signs of onset of GCA, or has led to the diagnosis of GCA
    2. either or both of the following:
        a. headache has significantly worsened in parallel with worsening of GCA
        b. headache has significantly improved or resolved within 3 days of high-dose steroid treatment
    3. headache is associated with scalp tenderness and/or jaw claudication
D. Not better accounted for by another ICHD-3 diagnosis.

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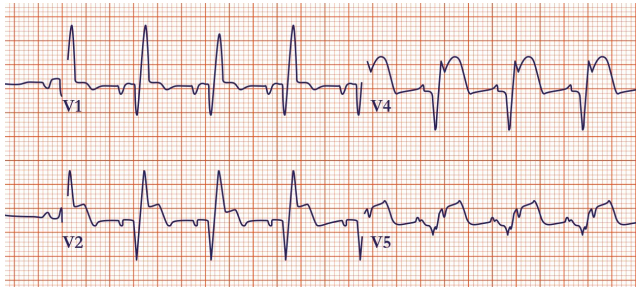
Cardiac Cephalalgia

A headache that often presents like migraine, usually but not always aggravated by exercise, occurring with an episode of myocardial ischaemia



ICHD-3 Diagnostic criteria:

A. Any headache fulfilling criterion C

B. Acute myocardial ischaemia has been demonstrated

C. Evidence of causation demonstrated by at least two of the following:
   1. headache has developed in temporal relation to the onset of acute myocardial ischaemia
   2. either or both of the following:
      a) headache has significantly worsened in parallel with worsening of the myocardial ischaemia
      b) headache has significantly improved or resolved in parallel with improvement in or resolution of the myocardial ischaemia
   3. headache has at least two of the following four characteristics:
      a) moderate to severe intensity
      b) accompanied by nausea
      c) not accompanied by photophobia or phonophobia
      d) aggravated by exertion
   4. headache is relieved by nitroglycerine or derivatives of it

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

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