Chapter 6
Diagnosis of Major Secondary Headaches 1, the Basics, Head and Neck Trauma, and Vascular Disorders

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Introduction

Headaches attributable to another disorder are classified as secondary headaches.

If during the investigation, no underlying disorder or disease process can be identified, the headache is then considered a primary headache.

The most common primary headache disorders include migraine, tension-type headache, and cluster headache. Although primary headaches are what are most often encountered in clinical practice, concern for secondary causes often requires that the clinician initiate an appropriate investigation with laboratory and neuroimaging studies.

There are numerous causes of secondary headaches, classified into eight groups by the International Classification of Headache Disorders, 3rd edition, beta version (ICHD-3); see Table 6.1). In order to cover the investigation and treatment of secondary headaches, two chapters have been set aside. Chapter 6 covers the basics of when to work up the possibility of secondary headaches, and also examines headaches stemming from head and neck trauma and vascular disorders. Chapter 7 covers secondary headaches caused by nonvascular disorders. Chapter 7 will also review those headaches not considered to be a primary headache disorder which are classified under painful cranial neuropathies, other facial pains, and other headaches.

Diagnostic Criteria for Secondary Headaches

By definition, either a secondary headache must be in close temporal relation to another disorder or there is evidence of a causal relationship (Table 6.2). Patients may present to the emergency department when a new headache is acute in onset or seek outpatient evaluation when the headache is subacute or chronic.

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Table 6.1 Secondary headaches and cranial neuralgias as classified by ICHD-3

- Headache attributed to trauma or injury to the head and/or neck
- Headache attributed to cranial or cervical vascular disorder
- Headache attributed to nonvascular intracranial disorder
- Headache attributed to a substance or its withdrawal
- Headache attributed to infection
- Headache attributed to disorder of homeostasis
- Headache or facial pain attributed to disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial or cervical structure
- Headache attributed to psychiatric disorder
- Painful cranial neuropathies and other facial pains
- Other headache disorders

Table 6.2 Diagnostic criteria for secondary headaches

A patient with secondary headache must have:

1. A disorder known to cause headaches
2. Two of the following in support of causation
   A. Headache onset temporally related to the onset of the presumed causative disorder
   B. Headache that improves or worsens in parallel with the improvement or worsening of causative disorder
   C. Characteristics of headache that are typical for the causative disorder
   D. Other evidence of causation is present, not specified
3. Headache cannot be attributed to another ICHD-3 diagnosis

It is easier to establish causation in acute onset headaches, but less so in those that are in a chronic pattern. Secondary headaches often lack defining features or may have characteristics that overlap with primary headaches. Causative disorders may also change the frequency or pattern of headache in an individual known to have a primary headache disorder. This can make the diagnosis of secondary headache challenging. Previously, the ICHD-2 criteria specified that the diagnosis of a secondary headache could be made only if the headache improved or remitted within 3 months of treatment of the causative factor. This stipulation is no longer required for diagnosis with the ICHD-3.

Clinical History of Secondary Headaches

Some patients with secondary headache have a preexisting history of primary headaches. Therefore, clinicians must be vigilant for any change in pattern, character, or overall worsening of the patient's headaches, as this may suggest a new secondary etiology.

Obtaining a detailed headache history is essential in the evaluation of secondary headaches. It is important to know whether the onset was preceded by an unusual event or provocation, whether there is a trend in pain intensity since onset, duration,

Table 6.3 The SNOOP mnemonic for red flags for secondary headache. (Adapted from Dodick 2003)

S ystemic symptoms (fever, weight loss) or
S econdary risk factors underlying disease (HIV, cancer, autoimmune disease)
N eurologic symptoms or abnormal signs (confusion, impaired alertness or consciousness, focal exam)
O nset: sudden, abrupt, or split-second (first, worst)
O lder age onset: new onset and progressive headache, especially in age > 50 (giant cell arteritis, cancer)
P attern change: first headache or different, change from
P revious headache history: attack frequency, severity or clinical features

associated symptoms, and particularly any reported focal neurological deficits. A workup is warranted in patients whose clinical history raises red flags or is atypical. As previously mentioned in Chap. 1, a useful mnemonic created by Dr. David Dodick for identifying red flags is "SNOOP" (Table 6.3).

Diagnostic Testing

Many patients, particularly those presenting with an episodic occurrence of a typical primary headache, do not warrant further investigation if their physical and neurological examinations are normal and no red flags are elicited in the history. Fortunately, less than 5 % of the patients presenting to the emergency department or physician's office with headache will be found to have significant underlying causative pathology. The majority of those pathological diagnoses are found in older individuals. In the pediatric population, it is even more unlikely to find an intracranial tumor as a cause of headache in the absence of any focal neurological signs or symptoms. Only a small percent of chronic headache suffers, ~ 1 %, will have significant findings on neuroimaging. Despite the relatively low odds of finding such pathology, clinicians still have to determine which patients, presenting with de novo or persistent headache, warrant investigation to uncover potentially treatable headache etiologies.

Some patients are so disabled by fear that a serious cause underlies their headache that investigation is appropriate to relieve their concerns. There are various medicolegal and managed care constraints that also influence ordering of diagnostic tests. Patients reporting typical common headache characteristics along with demonstration of a normal neurological examination may simply be reassured that the likelihood of finding an intracranial abnormality of significance, with imaging testing, is similar to the general population. The American Academy of Neurology (AAN) has published practice parameter guidelines for nonacute headache neuroimaging (Table 6.4) and the American College of Emergency Physicians (ACEP) has published recommendations for acute headache imaging (Table 6.5). These guidelines along with the clinician's clinical judgment can be helpful in deciding which patients warrant further testing.

Table 6.4 American Academy of Neurology (AAN) Guidelines: Neuroimaging recommendations for nonacute headache

Neuroimaging should be considered when:
• There are unexplained abnormal findings on the neurological examination
• Patients present with atypical headache features or headaches not meeting strict criteria for migraine or other primary headache disorders
• Patients have additional risk factors for secondary headache such as immunodeficiency, infection, neoplasm, or autoimmune disease
Neuroimaging is usually not warranted in patients with migraine and a normal neurologic examination
No evidence-based recommendations are established for the following:
• Presence or absence of neurologic symptoms alone
The following symptoms may indicate a higher likelihood of significant abnormality on neuroimaging, but absence did not lower the odds of this:
• Headache worsened by Valsalva maneuver
• Rapidly increasing headache frequency
• History of dizziness or lack of coordination
• History of subjective numbness or tingling
• History of headache causing awakening from sleep

Table 6.5 American College of Emergency Physicians (ACEP): Neuroimaging recommendations for acute headache

• Patients presenting to emergency rooms (ERs) with headache and new abnormal neurological signs (e.g., focal deficit, altered mental status, altered cognitive function) should undergo emergent[a] noncontrast head computed tomography (CT)
• Patients presenting with new sudden-onset severe headache should undergo emergent[a] head CT
• HIV-positive patients with a new type of headache should be considered for an emergent[a] neuroimaging study
• Patients who are older than 50 years and presenting with a new type of headache but with a normal neurologic examination should be considered for an urgent[b] neuroimaging study

[a] Emergent studies are those essential for a timely decision regarding potentially life threatening or severely disabling entities

[b] Urgent studies are those that are arranged prior to discharge from the emergency department

Diagnostic tests generally include imaging such as computed tomography (CT) or magnetic resonance imaging (MRI), and/or lumbar puncture (LP), and laboratory studies. Although routine blood tests are generally not useful in headache diagnosis, many clinicians order a baseline complete blood count (CBC) and chemistry profile (CMP) to include renal and liver function tests, along with a thyroid-stimulating hormone (TSH). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are useful to exclude the diagnosis of giant cell arteritis (GCA) in patients aged 50 years and above. Other laboratory tests which may be helpful depending on the clinical situation are listed in Table 6.6.

MRI is the imaging study of choice in most instances because of its increased sensitivity in detecting pathology, as well as its higher resolution for normal structures. MRI with gadolinium is advised when there is concern for an inflammatory or infectious process, brain tumor, demyelinating disease, or low cerebral spinal fluid

Table 6.6 Useful diagnostic tests in diagnosis secondary headaches

Test	Indication
CBC, CMP, TSH	• Baseline studies • Hypothyroidism/hyperthyroidism
ESR, CRP, antinuclear antibodies (ANA), rheumatoid factor (RF)	• Giant cell arteritis • Systemic lupus erythematosus • Rheumatologic conditions
Hypercoagulable panel, lupus anticoagulant, anticardiolipin antibodies	• Stroke • Cerebral venous thrombosis • Vasculitis • Extensive white matter abnormalities
HIV antibody, Lyme antibody	• Infectious disease
Toxicology screen	• Opioid abuse • Medication compliance • Vasculitis secondary to illicit substances
Carboxyhemoglobin level	• Carbon monoxide intoxication
Genetic testing	• NOTCH 3 gene (cerebral autosomal-dominant arteriopathy with subcortical infarcts and leukoencephalopathy, CADASIL) • Mitochondrial DNA (mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes, MELAS)
MRI with or without gadolinium (MRI generally preferred over CT)/ CT with or without contrast	• Tumor • Stroke • Hemorrhage: subarachnoid or intracranial • Hematoma: subdural or epidural • Chiari malformation • Vasculitis • Infection: encephalitis or meningitis
Magnetic resonance angiography (MRA)	• Aneurysm • Vascular dissection • Vascular malformation
Magnetic resonance venography (MRV)	• Cerebral venous thrombosis
Computer tomography angiography (CTA)	• Aneurysm, vascular dissection (higher sensitivity than MRA)
Computer tomography venography (CTV)	• Cerebral venous thrombosis
Conventional angiography	• Aneurysm • Vasculitis • Vascular dissection • Vascular malformation
Lumbar puncture	• Infection: meningitis or encephalitis • Carcinomatosis • Subarachnoid hemorrhage • Vasculitis • Idiopathic intracranial hypertension • Low CSF pressure headache
EEG	• Only indicated if concern for underlying seizure disorder associated with headache

headache. However, in the acute/emergency setting, or if contraindications to MRI exist, CT is still useful and will detect most abnormalities that cause headache.

Conventional cerebral angiography remains the best diagnostic tool for central nervous system vasculitis or for patients with subarachnoid hemorrhage (SAH). MR angiography/venography (MRA/MRV) and CT angiography/venography (CTA/CTV) are useful for detecting vascular lesions such as arterial stenosis, dissection, thrombosis, reversible cerebral vasoconstriction syndrome (RCVS), and aneurysm. CTA has a higher sensitivity than MRA in detecting cerebral aneurysms. When lesions are identified that require serial monitoring with repeat imaging, MRI is the preferred method due to risk of repeated radiation exposure with CT.

Electroencephalography (EEG) is only recommended in patients with headache who also report symptoms that may be suggestive of a seizure. EEG is no longer indicated in the routine evaluation of headache as a means to exclude a structural lesion.

In patients presenting to the ER with sudden-onset, severe headache and a negative noncontrast head CT scan result, LP should be performed to rule out SAH. The timing of the LP is important when interpreting results, as results may be falsely negative when performed within 12 h of onset of bleeding. Patients with signs of meningeal irritation should undergo an LP to exclude meningitis/encephalitis. As a general rule, cerebrospinal fluid (CSF) white blood cells (WBCs) should be less than 5, with 1 additional WBC allowed for each 700 red blood cells (RBCs) in the case of a traumatic tap. CSF protein is also elevated in the presence of RBCs, with an increase of 1 mg/dL for every 750 RBCs. CSF glucose should be two-thirds of serum glucose level.

Headache Attributed to Trauma or Injury to the Head and/or Neck

Following trauma to the head or neck, it is not uncommon for patients to report the onset of new headache. Headache attributed to trauma or injury to the head and/or neck may be associated with mild, moderate, or severe head injury, whiplash-type injuries, as well as following craniotomy. Traumas may worsen preexisting headache conditions. Post-traumatic headache (PTHA) is frequently associated with other somatic, psychological, and cognitive symptoms which are referred to as post-concussion syndrome or post-traumatic syndrome in those who did not suffer a concussion (Table 6.7). PTHA and concussion are covered more extensively in Chap. 24, but will be discussed briefly here.

The risk for developing PTHA and post-concussion syndrome seems to be inversely related to the severity of head injury. Other risk factors include female gender, prior known headache disorder, as well as history of psychiatric disease. The mechanism and pathophysiology behind PTHA and this post-concussion syndrome is not well understood. It is likely that axonal injury along with changes in brain metabolism and blood flow can contribute to PTHA, particularly in individuals with

Table 6.7 Features of post-concussion/post-traumatic syndrome

- Headache: tension-type, migraine, cluster, cervicogenic, occipital neuralgia
- Dizziness/vertigo
- Nausea/vomiting
- Tinnitus/hearing loss
- Blurred vision
- Anosmia
- Photophobia and/or phonophobia
- Orthostatic intolerance/dysautonomia
- Fatigue
- Disturbed sleep: insomnia, nonrestorative sleep, and hypersomnolence
- Memory loss/poor concentration
- Impaired libido
- Personality changes: apathy, anger, irritability
- Depression/anxiety

a genetic predisposition or premorbid conditions. Recent scientific evidence with more sophisticated imaging has demonstrated structural abnormalities to the brain even with minor head injuries.

Acute headache attributed to trauma or injury to the head and/or neck by ICHD-3 beta definition occurs within 7 days of the head or neck trauma (or within 7 days of when the patient regains consciousness or is able to feel pain and report it), and resolves within 3 months. Persistent headache attributed to trauma or injury to the head and/or neck is diagnosed when the headache following injury fails to resolve after 3 months' time. This was previously referred to as chronic PTHA. The post-traumatic headaches are also classified according to the severity of injury, mild, moderate, or severe. Cases in which headache onset is delayed greater than 7 days following injury should be noted as such by the clinician.

Clinical features of PTHA are not specified by the ICHD-3 beta, and are similar to the primary headache disorders, most frequently tension-type headache. Patterns similar to migraine, cluster headache, cervicogenic headache, and a variety of other headache types have been noted as well. These patients are at risk of medication-overuse headache (MOH), and development of this secondary etiology should be considered in persistent cases. The role that litigation or malingering plays in persistence of symptoms is still undetermined.

Headaches Associated with Vascular Disease

Headache is a relatively common symptom in a variety of underlying cerebrovascular diseases (Table 6.8). Intracranial hemorrhages are most often associated with an abrupt onset of severe headache, termed "thunderclap" headache. Thunderclap headache is defined as a severe headache reaching maximal intensity within seconds

Table 6.8 Vascular diseases associated with headache

Vascular pathology	Vascular diagnosis
Ischemic	• Ischemic stroke
	• Transient ischemic attack
Intracranial hemorrhage	• Intracerebral hemorrhage
	• Subarachnoid hemorrhage
Unruptured vascular malformation	• Saccular aneurysm
	• Arteriovenous malformation
	• Arteriovenous fistula
	• Cavernous angioma
Arteritis	• Giant cell arteritis
	• Primary central nervous system angiitis
Carotid or vertebral artery pain	• Cervical arterial dissection
	• Post-carotid endarterectomy headache
	• Post-angioplasty headache
	• Post-stenting headache
	• Post-coiling/clipping headache
Venous thrombosis	• Cerebral venous thrombosis
Other vascular disorders	• CADASIL
	• MELAS
	• Reversible cerebral vasoconstriction syndrome (RCVS)

to a minute. Headaches may be a consequence of stroke, particularly hemorrhagic infarction. Migraine is also a known risk factor for stroke or vascular dissection.

Headache-Attributed Stroke and Transient Ischemic Attacks

Headache may be reported in 10–30 % of patients presenting with an acute ischemic stroke and less commonly in transient ischemic attacks (TIAs). Distinguishing the focal neurologic deficit of a TIA from a migraine aura can be challenging. Deficits associated with a TIA are sudden in onset versus those related to a migraine aura, which tend to develop over 15–20 min. Headaches can also occur in association with strokes related to large-vessel atherothrombotic disease, cardioembolism, and to a lesser extent small-vessel atherothrombotic disease resulting in lacunar infarcts (Table 6.9).

The symptoms of TIA-related headache may develop just prior to or concurrent with the development of focal neurologic deficits. There are no defining characteristics of the headache associated with ischemia, but they tend to be of moderate intensity.

Ischemia in the distribution of the posterior circulation is more likely to produce headaches than ischemia involving the anterior circulation. The headache pain is often unilateral, occurring on the same side of the stroke. A stroke patient who develops progression of neurologic deficits along with new-onset headache must be reevaluated for hemorrhagic transformation of the area of ischemia (Table 6.10).

Table 6.9 Clinical pearls on distinguishing TIAs versus migrainous aura

- Onset of symptoms in a TIA is usually sudden; aura is usually gradual over 15–20 min
- Duration of TIAs is brief, usually lasting from seconds to minutes; average duration of aura is 20–30 min up to an hour
- TIAs usually present with negative symptoms (curtain coming down); auras with positive or mixed symptoms (zigzags, scintillating scotoma)

Table 6.10 Clinical pearls on headache and stroke

- Ischemia in the distribution of the posterior circulation is more likely to produce headaches than ischemia involving the anterior circulation
- Headache pain is often ipsilateral to the side of the stroke
- A stroke patient who develops progression of neurologic deficits along with new-onset headache must be reevaluated for hemorrhagic transformation of the area of ischemia

Headache Attributed to Intracranial Hemorrhage

For patients presenting with acute focal neurologic deficits consistent with a stroke pattern, the concurrent report of sudden headache raises great concern for the presence of an intracranial hemorrhage (ICH). Indeed, headache is reported in up to 70 % of patients diagnosed with ICH. The headache is most severe on the day of onset, localized to the side of hemorrhage, and tends to resolve with clinical improvement. Hemiparesis and decreased consciousness are associated clinical findings. Hypertension and advanced age are the two most significant risk factors for ICH. Headaches associated with ICH are more severe in nature than those associated with ischemic stroke.

Headache Attributed to Subarachnoid Hemorrhage (SAH)

Patients with subarachnoid hemorrhage (SAH) usually present with the sudden onset of "the worst headache of my life" or thunderclap headache. Thunderclap headache was covered in Chap. 3, but because of its importance and the frequency with which it is a secondary and not a primary headache, it is reviewed again here. The headache may be associated with alteration of consciousness, vomiting, photophobia, drowsiness, agitation, or neck stiffness. In 50 % of patients, an unruptured aneurysm may produce a warning headache referred to as a sentinel headache. Sentinel headaches occur in the days to weeks prior to aneurysm rupture.

Although thunderclap headache is the classic presentation of rupture of a saccular aneurysm resulting in SAH, many other diagnoses can have an abrupt presentation as well (Table 6.11). Diagnosis is confirmed by an emergent CT and/or lumbar puncture. Cerebral angiography is usually needed to identify the source of the hemorrhage (Table 6.12).

Spontaneous SAH occurs when aneurysms reach 7–10 mm in size. Aneurysmal rupture increases in risk with age, with a mean incidence of 50 years, and rarely

Table 6.11 Differential diagnosis of thunderclap headache

Secondary headaches	Primary headaches
– SAH	– Primary thunderclap headache
– Sentinel leak	– Primary exertional headache
– Unruptured cerebral aneurysm	– Primary cough headache
– Intracranial hemorrhage	– Primary sexual headache
– Cerebral venous thrombosis	
– Cervical artery dissection	
– Acute hypertensive crisis	
– Posterior reversible leukoencephalopathy syndrome (PRES)	
– Reversible cerebral vasoconstriction syndrome (RCVS)	
– Primary Angiitis of the Central Nervous System (PACNS)	
– Pituitary apoplexy	
– Spontaneous intracranial hypotension	
– Infection: meningitis, sinusitis	

Table 6.12 Clinical pearls in diagnostic evaluation of subarachnoid hemorrhage (SAH)

- Sensitivity of noncontrast CT scan in the diagnosis of SAH
  - < 12 h: 98 %
  - 24 h: 93 %
  - 7 days: 50 %
- Spectrophotometry is able to detect xanthochromia in CSF in 100 % of cases when collected between 12 h and 2 weeks after symptom onset

occurs before 20 years of age. SAH is considered a neurosurgical emergency with a high morbidity and mortality rate. A high index of suspicion is required to avoid misdiagnosis, which has been reported to occur in as much as 25–50 % of patients.

Giant Cell Arteritis (GCA)

Giant cell arteritis (GCA), formerly known as temporal arteritis, is a vasculitis of large- and medium-sized arteries that affects the elderly. The inflammation predominantly involves extracranial branches of the carotid artery, especially the temporal artery.

GCA exclusively occurs in individuals over the age of 50 years, and the incidence increases with age. Women are more likely to be affected than men. It is rare in African-Americans.

Classical symptoms of GCA include headache, scalp tenderness, jaw claudication, and visual loss if untreated. An elevated ESR (> 50 mm/h) is suggestive of the diagnosis, and the ESR is rarely normal, most often early in the disease (Table 6.13). Transcranial Doppler ultrasonography may be useful in confirming the diagnosis, but temporal artery biopsy remains the gold standard for diagnosis.

Table 6.13 American College of Rheumatology's diagnostic criteria for giant cell arteritis

- Age 50 years or older
- Newly onset localized headache
- Temporal artery tenderness or decreased temporal artery pulse, unrelated to arteriosclerosis of the arteries
- ESR > 50 mm/h
- Abnormal artery biopsy specimen characterized by mononuclear infiltration or granulomatous inflammation, usually with multinucleated giant cells

Some patients with GCA have myalgias consistent with the related inflammatory disorder, polymyalgia rheumatica. Prompt treatment with corticosteroids for GCA can prevent permanent visual loss which is the result of anterior ischemic optic neuropathy. The headache associated with GCA will dramatically improve or resolve within 3 days of high-dose steroid treatment.

Primary Angiitis of the Central Nervous System (PACNS) and Reversible Cerebral Vasoconstriction Syndrome (RCVS)

Primary angiitis of the central nervous system (PACNS) is a rare form of central nervous system (CNS) vasculitis. Common presenting symptoms include headache along with altered mental status. It is not uncommon for patients to go undiagnosed for 6 months or more due to the fact that other focal neurologic signs are less common at onset. Situations that should trigger consideration and possible investigation for possible PACNS would include multiple infarcts in different vascular territories, headache associated with cognitive changes, and chronic aseptic meningitis (Table 6.14).

This condition typically affects males over the age of 50 years. In contrast to other primary systemic vasculitides, serologic markers of inflammation are typically normal. MRI of the brain may demonstrate nonspecific white matter changes. CSF studies may also be nonspecific, revealing a modest elevation in total protein as well as a modest lymphocytic pleocytosis. Conventional angiography may be useful in diagnosing by demonstrating "beading" as evidence of segmental arterial narrowing, but confirmatory diagnosis with leptomeningeal and brain biopsy is often necessary. Once diagnosis is confirmed, immunosuppressive treatment is initiated with either corticosteroids and/or cyclophosphamide.

Reversible cerebral vasoconstriction syndrome (RCVS) is a syndrome that can be difficult to distinguish from primary CNS angiitis, because presenting signs and symptoms are similar. Angiography in both disorders demonstrates segmental narrowing but in RCVS this is related to vasospasm. Imaging of brain parenchyma can be normal in RCVS, but when infarcts occur, they are typically larger than those as a result of PACNS. Intracranial hemorrhage can be associated with RCVS but is not typical of PACNS. The correct diagnosis is critical, because RCVS patients are treated with calcium channel blockers, and CNS angiitis is often treated with cytotoxic therapy. The outcome is more favorable for RCVS (Table 6.15).

Table 6.14 Differential diagnosis of primary angiitis of the central nervous system (PACNS). (Adapted from Ju 2010 and Hajj-Ali 2013)

Noninflammatory vasculopathies
- Cerebrovascular atherosclerotic disease
- RCVS
- Fibromuscular dysplasia (FMD)
- Moyamoya
- CADASIL
- MELAS
- Hypercoagulable state

Infections
- Emboli from subacute bacterial endocarditis (SBE)
- Basilar meningitis caused by tuberculosis (TB) or fungal infection (aspergillosis, nocardiosis, cryptococcus, histoplasmosis)
- Bacterial or viral meningoencephalitis (syphilis, Lyme, HSZ, HIV)

Demyelinating syndromes
- Multiple sclerosis (MS)
- Acute disseminated encephalomyelitis (ADEM)

CNS vasculitis, secondarily affected as part of a primary vasculitis
- Large-vessel vasculitis (e.g., GCA, Takayasu arteritis)
- Medium-vessel vasculitis (e.g., polyarteritis nodosa, Kawasaki disease)

Small-vessel vasculitis
- Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (e.g., Wegener's granulomatosis)
- Churg–Strauss syndrome, microscopic polyangiitis
- Immune complex deposition (e.g., Henoch–Schönlein purpura, cryoglobulinemia)

Other systemic inflammatory conditions
- Neuro-Behcet's disease
- Systemic lupus erythematosus
- Scleroderma
- Sjogren's syndrome
- Crohn's disease
- Cogan's syndrome
- Sarcoid granulomatosis and angiitis
- Susac's syndrome

Neoplasms
- Primary CNS lymphoma
- Lymphomatoid granulomatosis
- Meningeal carcinomatosis
- Gliomatosis cerebri

Cerebral Venous Thrombosis

Thrombosis within the cerebral venous system most often is associated with a headache that is acute to subacute in onset. The headache pain is generally described as severe, diffuse, and constant in nature, but has occasionally been described as thunderclap in onset. The headache is worsened by recumbency or Valsalva-type maneuvers such as coughing or sneezing.

Table 6.15 Clinical features of primary angiitis of the central nervous system (PACNS) and reversible cerebral vasoconstriction syndrome (RCVS)

Characteristics	PACNS	RCVS
Demographics		
• Age range	40–60	20–40
• Sex	Males	Females
Clinical symptoms		
• Headache	Insidious, progressive	Acute, thunderclap
• Focal neurological symptoms	Yes, later in disease course	Yes, at onset
Provocative factors (migraine, pregnancy, medicines)	No	Yes
MRI	Nonspecific white matter changes	Normal
	Infarct	Infarct
	Mass lesion	Hemorrhage: ICH, SAH
	Hemorrhage: ICH, SAH	Posterior reversible encephalopathy syndrome (PRES)
	Gadolinium enhancement	
Angiogram	Beading, irregularity, often irreversible	Reversible vasospasm
Treatment	Corticosteroids	Calcium channel blockers
	Cyclophosphamide	

This disorder typically affects children or young adults, and women much more frequently than men (Table 6.16). Obstruction of the venous sinuses results in intracranial hypertension and thrombosis. This may eventually lead to venous infarctions which tend to undergo hemorrhagic transformation. Focal neurologic signs, encephalopathy, or seizures commonly accompany the onset of headache.

Patients with cortical vein thrombosis may present very similarly to idiopathic intracranial hypertension (pseudotumor cerebri, IIH) with signs and symptoms of dizziness, tinnitus, diplopia, and visual obscurations. Papilledema may be found on examination.

Risk factors for cortical vein thrombosis include hypercoagulable states, pregnancy, use of oral contraceptives and dehydration. Venous thrombosis may be diagnosed through MRV or CTV. The recommended duration of treatment with anticoagulation for cerebral venous thrombosis is 6 months. However, the headache generally resolves within 1 month of the initiation of treatment.

Headache Attributed to Carotid or Vertebral Artery Pain

Spontaneous dissection of the vertebral or carotid artery may produce head pain. The diagnosis should be considered in individuals reporting new onset of head pain along with neck pain. Clinical suspicion should be raised if the patient endorses a recent history of known provocative factors such as chiropractic adjustment, severe vomiting, and neck trauma including whiplash-type injuries. Patients with colla-

Table 6.16 Clinical pearls on cerebral venous thrombosis

Characteristics	Findings
Demographics	
• Sex	Women > Men
• Age	Children, young adults
Headache	
• Onset	Acute to subacute
• Description	Throbbing, band like, thunderclap
	Worsened by Valsalva
Clinical symptoms	Seizures
	Encephalopathy
	Nausea and vomiting
	Papilledema
	Cranial nerve palsy
	Diplopia, visual obscurations
	Tinnitus
	Focal findings related to stroke
Complications	Venous infarction
	Hemorrhagic transformation (Parenchymal > subarachnoid, subdural)
Risk factors	Hypercoagulable state
	Oral contraceptives
	Pregnancy
	Dehydration
	Infection: sinusitis, mastoiditis, otitis
	Trauma
	Inflammatory/rheumatologic disease
Evaluation	CBC
	Hypercoagulable profile
	Antiphospholipid/anticardiolipin antibodies
	ESR, CRP, ANA
	MRV/CTV
	EEG
Treatment	Anticoagulation
	Interventional angiography: thromobolytic therapy in severe cases

gen vascular disease or fibromuscular dysplasia are at particular risk. The headache tends to be ipsilateral to the side of dissection (Table 6.17).

Location of pain is frontal for carotid dissections and more occipital for vertebral dissections. Carotid artery dissection may manifest clinically with a Horner's syndrome or amaurosis fugax. Vertebral artery dissection may produce vertebrobasilar symptoms, especially a Wallenberg syndrome (difficulty with swallowing, hoarseness, dizziness, nausea, nystagmus, gait and balance abnormalities, and sensory and motor deficits, sometimes on opposite sides). Patients should undergo diagnostic evaluation with an MRI/MRA with a fat-saturation protocol, CT angiogram, or conventional angiography, which will also help identify secondary complications such as stroke or pseudoaneurysm formation.

Headache has been reported following carotid endarterectomy, carotid clipping, and other endovascular procedures including angioplasty, coiling, embolization,

Table 6.17 Clinical pearls on headache and dissection

Characteristics	Findings
Headache	
• Onset	Acute to subacute
• Description	With neck pain
	Headache is ipsilateral to side of dissection
	Frontal pain for carotid dissection
	Occipital pain for vertebral dissection
Clinical symptoms	Horner's syndrome for carotid dissection
	Amaurosis fugax/transient monocular blindness for carotid dissection
	Vertebrobasilar symptoms, especially a Wallenberg syndrome for vertebral dissection
Risk factors	Chiropractic adjustment
	Severe vomiting
	Neck trauma including whiplash-type injuries
	Collagen vascular disease or fibromuscular dysplasia
Evaluation	MRI/MRA with a fat-saturation protocol, CT angiogram, or conventional angiography (also helps identify secondary complications such as stroke or pseudoaneurysm formation)
Treatment	Anticoagulation

and stenting. The headache begins in the first few days after surgery but often resolves within the month of onset.

Post-carotid endarterectomy headache follows three pain patterns unilateral and ipsilateral to the side of surgery:

1. Diffuse mild pain
2. Cluster headache-like pain
3. Severe and pulsating pain

Preexisting headache conditions may be a risk factor for these post-procedural headaches. The mechanism can be related to a hyperperfusion syndrome following improved blood flow or manipulation of intracranial vessel resulting in activation of the trigeminovascular system.

Pituitary Apoplexy

Pituitary apoplexy is an important syndrome to recognize, as it can be a life-threatening emergency. It is the result of hemorrhage or infarction of the pituitary gland, most often in patients with a pituitary adenoma. Patients report the abrupt onset of a severe headache along with symptoms of vision loss, ophthalmoplegia, and mental status change. Serious complications include adrenal crisis, coma, and even death. MRI is the most sensitive imaging study for detection of pituitary apoplexy (Table 6.18).

Table 6.18 Clinical pearls on pituitary apoplexy

- Severe acute retro-orbital, frontal, or diffuse headache accompanied by at least one of the following symptoms:
  - Nausea and vomiting
  - Fever
  - Altered level of consciousness
  - Hypopituitarism
  - Hypotension
  - Ophthalmoplegia or impaired visual acuity
- Evidence of acute hemorrhagic pituitary infarction
- Symptom resolution within 1 month

Conclusions on Diagnosis of Secondary Headaches

- Use the SNOOP mnemonic (Table 6.3) to decide when to workup patients with headache for secondary causes
- MRI is generally superior to CT in working up secondary headaches
- Post-traumatic headaches begin within 1 week of the injury, according to the ICHD-3 beta, and have no required clinical features
- Headaches associated with TIA, stroke, and dissection are usually ipsilateral to the event
- TIAs can usually be distinguished from migrainous aura by sudden onset, negative features, and briefer duration
- Always work up headache in the elderly with a sedimentation rate and CRP for GCA

Suggested Reading

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