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AUTHORS

Murtaza Akhter, MD, Assistant Professor, Department of Emergency Medicine, University of Arizona College of Medicine–Phoenix, Maricopa Integrated Health System, Phoenix, AZ.

Daniel R. Dobbe, MD, Department of Emergency Medicine, Maricopa Integrated Health System, Phoenix, AZ.

Daniel Orosco, DO, Department of Emergency Medicine, Maricopa Integrated Health System, Phoenix, AZ.

Levi Filler, DO, Department of Emergency Medicine, Maricopa Integrated Health System, Phoenix, AZ.

PEER REVIEWER

Larry B. Mellick, MD, MS, FAAP, FACEP, Department of Emergency Medicine, Augusta University, Augusta, GA.

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Sudden Onset Headache

Introduction

Roughly 2% of patients will present to the emergency department (ED) with a chief complaint of atraumatic headache.[1] The majority of these patients will have benign conditions underlying their pain, but 2-4% of these patients, or approximately one in 25, will have a high-risk etiology to their headache.[2] The estimated incidence of those who describe their headache as "thunderclap" in quality is 43 per 100,000 adults per year in the developed world.[3,4] The term thunderclap was first used by Day and Raskin when describing this type of headache in the setting of an unruptured cerebral aneurysm.[5,6] Since its introduction, it has evolved into a term associated with more ominous causes of headache.

Thunderclap headaches are described as severe and instantaneous, with peak severity within up to 60 seconds of symptom onset.[3,5] Historically, given the association with various life-threatening etiologies, these headaches warrant prompt and thorough investigation. The description of a thunderclap headache classically is associated with subarachnoid hemorrhage (SAH); however, one study found that only 11.3% of thunderclap headaches are due to SAH.[4] Many other conditions present similarly, but given the morbidity and mortality associated with the various causes of thunderclap headache, a life-threatening intracranial etiology should be considered in these patients. The timeframe of headache onset is paramount during evaluation and history by the emergency provider. Although the classic definition cites one minute as the timeframe for maximal intensity, some may consider one hour as the appropriate timeframe for considering a headache as sudden onset.[7-9] Like SAH, many other causes of sudden onset headache are vascular in etiology and are among the most sinister. Among these are pituitary apoplexy, cerebral venous sinus thrombosis (CVST), cervical artery dissection, ischemic stroke, hypertensive crisis, and reversible cerebral vasoconstriction syndrome.

The International Headache Society (IHS), formed in 1981, created the International Classification of Headache Disorders (ICHD) to further categorize the various causes and presentations of headache. The ICHD divides headaches into primary and secondary disorders.[10] According to the ICHD, a diagnosis of a primary headache disorder requires the exclusion of a secondary cause.[3,11] The majority of sudden onset headaches are related to secondary causes of headache, which are manifestations of a separate disease process and have the potential to cause significant morbidity and mortality if not properly evaluated in a timely manner. Furthermore, secondary causes of thunderclap headaches can be subdivided into vascular and nonvascular causes. (*See Table 1.*) Some primary headache disorders also can be described as sudden onset and, although important to recognize, rarely have life-threatening sequelae (i.e., exertional headache, post-coital headache, etc.).

EXECUTIVE SUMMARY

- Subarachnoid hemorrhage (SAH) is more common in patients with a first-degree relative with a history of cerebral aneursym, and in patients with polycystic kidney disease, Marfan syndrome, or Ehlers-Danlos syndrome.
- While the classic workup for SAH has been computed tomography (CT) followed by lumbar puncture if the CT is negative, recent studies show that CT, with a modern machine, within six hours of the onset of headache can accurately rule out an SAH.
- Patients with cerebral venous sinus thrombosis often have a prior history of hypercoagulable disorders, pregnancy, systemic inflammatory disease, connective tissue disease, or take oral contraceptives. It is often called the deep vein thrombosis of the brain.
- In addition to SAH, other causes of thunderclap headache include cerebral venous sinus thrombosis, pituitary apoplexy, ischemic stroke, cervical artery dissection, acute hypertensive crisis, reversible cerebral vasoconstriction syndrome, spontaneous intracranial hypotension, retroclival hematoma, colloid cyst of the third ventricle, primary thunderclap headache, and post-coital headache/exertional headache/primary cough headache.

This article will outline the presentation of sudden onset headache in the ED, with a focus on important history and physical examination findings, associated differential diagnoses, and the appropriate workup and treatment of each condition.

History

The history is perhaps the most important aspect when approaching a patient with a headache. As with other maladies, it is important to characterize the quality, location, severity, onset, duration, and surrounding events.

When evaluating a patient for a headache, there is always the possibility of referred pain from caudal structures.[12] Headaches can be caused by injury or disease affecting the ligaments, muscles, and joints in the upper cervical spine.[12] However, this referred pain rarely presents with a thunderclap headache.

Obtaining the history requires patience and finesse. Providers can convince themselves that the patient's pain was not maximal at onset and forge down the wrong path. Allow time for the patient to explain the progression of the headache. What caused the patient to visit the ED? How long has the pain been this severe? What is the quality of the headache? Does it throb or pulse? Is there constant severe pressure? These questions in the diagnosis must be used cautiously as they can be misinterpreted. History and presentation will vary as we progress through the different conditions outlined. Many of these patients will describe excruciating pain that has not improved with common over-the-counter treatments.

Vascular Causes

Subarachnoid Hemorrhage

SAH is one of the most well-known, life-threatening causes of thunderclap headache. SAH often is described as a thunderclap headache because of its abrupt nature of onset and severity. Even though SAH is well-known and described in the literature, only 1% of patients presenting to the ED with a headache have an SAH.[9,13] The history is crucial to the diagnosis of SAH. The provider should be cognizant of potential "red flag" signs of the headache, with characteristics of onset and severity being of utmost importance.

A 2002 study with 173 consecutive patients who presented with sudden onset headache, attempted to delineate common features associated with SAH. The researchers found that nausea, neck stiffness, occipital location, and impaired consciousness were significantly more frequent with SAH.[4] Although many features in the history and physical exam can increase the risk of SAH, virtually none are specific or sensitive enough to rule in or rule out the disease.[14-17] However, the sudden onset nature of the headache is virtually the sine qua non of SAH;[14-16] patients presenting with sudden onset headache, regardless of severity, should be evaluated for potential SAH.[16,18]

Aside from described symptoms in the ED, past medical history and family history may reveal underlying risk factors that would predispose the patient to SAH. According to Van Gijn et al, approximately 86% of SAH are from ruptured intracranial saccular aneurysms, with 11% caused by perimesencephalic syndrome and the remainder by AV anomalies and rare causes.[19] It has been well described that intracranial aneurysms may follow a familial pattern via various genetic mechanisms. According to a study by Schievink et al, 15 out of 76 patients (20%) had a first- or second-degree relative with aneurysmal SAH.[20,21] Other genetic factors also are known to play a role in the development and rupture of SAH such as autosomal dominant polycystic kidney disease, Marfan syndrome, and Ehlers-Danlos syndrome type IV, among other postulated inherited genetic defects.[21] Along with associated symptoms and family history, other factors should be considered when assessing for SAH, including female gender, hypertension, atherosclerosis, diabetes, and vascular anatomic differences. These additional findings are thought to be implicated in the pathogenesis of aneurysms.[22,23]

Physical Exam/Presentation. Because SAH is likely the most studied entity under the umbrella of thunderclap headache, scales have been created to grade a patient's presentation. There are a couple of clinical scales and numerous radiological scales. The clinical scales are summarized below:

Hunt and Hess Scale[24]

- Mild headache, normal mental status, no cranial nerve or motor findings;
- Severe headache, normal mental status, may have cranial nerve deficit;
- Somnolent, confused, may have cranial nerve or mild motor deficit;
- Stupor, moderate to severe motor deficit, may have intermittent reflex posturing;
- Coma, reflex posturing or flaccid.

Table 1. Key Clinical Features of Vascular and Nonvascular Causes of Thunderclap Headache

Vascular Causes	Characteristics
Subarachnoid hemorrhage	Neck stiffness, neurologic signs, altered level of consciousness
Cerebral venous sinus thrombosis	Female to male predominance; can present with focal neurologic deficits and seizures
Pituitary apoplexy	Associated with known pituitary adenoma; can have visual symptoms and cranial nerve deficits
Ischemic stroke	Uncommon, presents with focal neurologic deficits
Cervicocephalic arterial dissection	Can present with Horner's syndrome
Acute hypertensive crisis	Extreme blood pressure elevations, signs of end organ damage
Reversible cerebral vasoconstriction syndrome	Recurrence of thunderclap headache
Nonvascular Causes	**Characteristics**
Retroclival hematoma	Pediatric predominant; precipitated by minor trauma; associated with atlantoaxial dislocation
Colloid cyst of the third ventricle (post fossa mass)	Can be associated with other symptoms of obstructive hydrocephalus (i.e., gait ataxia, confusion)
Primary thunderclap headache	Indistinguishable from secondary causes; diagnosis of exclusion
Post-coital headache	Explosive headache occurring just before or during orgasm
Exertional headache	Associated with sustained physical exertion, lasts < 48 hours
Primary cough headache	Brief, associated with straining maneuvers (i.e., Valsalva, cough); Chiari malformation associated
Spontaneous intracranial hypotension	Postural; worse with standing and improved with supine position

World Federation of Neurological Societies (WFNS) 1998.[25]

- Grade 1: Glasgow Coma Scale (GCS) score 15, no motor deficits;
- Grade 2: GCS score 13-14, no motor deficits;
- Grade 3: GCS score 13-14, with motor deficits;
- Grade 4: GCS score 7-12, with or without motor deficits;
- Grade 5: GCS score 3-6, with or without motor deficits.

As implied from the scales listed above, SAH may present with cranial nerve abnormalities, which may occur prior to motor nerve deficits. Although the Glasgow Coma Scale was introduced for trauma patients, it is a component of the WFNS scale, which helps communicate the patient's severity to other care teams.

There are no pathognomonic signs or symptoms of SAH. Studies have found that seizures and diplopia were the only two features that occurred exclusively in aneurysmal SAH; however, their frequency was not high enough to be of predictive value.[4,26] According to a literature review by Carpenter et al, the symptoms with the most positive likelihood ratios for SAH are neck pain (positive likelihood ratio [LR+] 4.1; 95% confidence interval [CI], 2.2-7.6) and neck stiffness on exam (LR+, 6.6; CI, 4.0-11.0).[27] Interestingly, photophobia and blurred vision were present in less than 10% of patients diagnosed with SAH. These may be more common in migraines.

Terson syndrome is when SAH is accompanied by a vitreous hemorrhage.[4] According to a 2004 systematic review, this sign was found prospectively in 13% of 181 patients.[28] This number was lower in the retrospective studies examined. Notably, those with Terson syndrome had a higher Hunt and Hess score and higher mortality.[28] Despite some associations, it is important to understand that there are no pathognomonic symptoms or signs that allow a reliable differentiation between SAH and non-SAH forms of thunderclap headache.[4]

Diagnosis. SAH should be at the forefront of the emergency practitioner's differential diagnosis of thunderclap headache. As with any disease entity, a focused history and physical is paramount to identifying SAH. In particular, it is critical to ascertain whether the headache was truly thunderclap in nature.

The standard approach to evaluating SAH involves a computed tomography (CT) scan of the head followed by lumbar puncture (LP) if the CT is negative for SAH. This approach has been validated, with 100% sensitivity, and is a recommendation in the Clinical Policy of the American College of Emergency Physicians (ACEP)[29] as well as the American Heart Association (AHA) and American Stroke Association (ASA).[30]

Continuous advancements in the technology of CT make the traditional teaching of identifying xanthochromia on LP increasingly obsolete.[27,30] Recent studies have demonstrated diagnostic sensitivity of third-generation noncontrast head CT scans approaching 100% when performed within the first six hours of headache onset and when interpreted by a qualified radiologist.[8] Furthermore, xanthochromia also is an insensitive test for ruling in SAH, even beyond the six-hour time mark.[31-36] A recent study, however, found that no xanthochromia and red blood cell count < 2000×10^6/L (same as < 200 red blood cells/mm^3) was 100% sensitive in ruling out SAH.[7]

Table 2. Differential Diagnosis

Vascular Related Causes
• Subarachnoid hemorrhage
• Cerebral venous sinus thrombosis
• Pituitary apoplexy
• Ischemic stroke
• Cervical artery dissection
• Acute hypertensive crisis
• Reversible cerebral vasoconstriction syndrome
Nonvascular Related Causes
• Spontaneous intracranial hypotension
• Retroclival hematoma
• Colloid cyst of the third ventricle
• Primary thunderclap headache
• Post-coital headache/exertional headache/primary cough headache

Some studies have assessed the potential of CT angiography (CTA) to supplant LP in sudden onset headache patients with a negative CT.[37-43] The ACEP and AHA/ASA guidelines still recommend the CT/LP approach as of now,[29,30] but many experts recommend a shared decision-making approach to patients who present with sudden onset headache and a negative head CT.[44-46]

Treatment. As with many disease processes, supportive care is the cornerstone of management of SAH in the acute setting.[47,48] As a true medical emergency, disposition will focus on stabilization with subsequent hospital admission, ideally to a specialized neurosurgical critical care unit.

Airway protection with endotracheal intubation may be indicated depending on the severity of presentation.[49,50] A 2016 literature review by Bucher and Koyfman found no evidence that pretreatment with lidocaine prior to rapid sequence intubation decreased intracerebral pressure. Adjunctive medication, such as fentanyl, can be considered to blunt hemodynamic response to intubation. Ketamine's relatively stable effects on hemodynamics may prove useful as an induction agent.[50]

In addition to correction of hypoxemia, blood pressure management (avoiding hypotension or severe hypertension) is a cornerstone of therapy, although studies have shown variable effects on morbidity and mortality. The INTERACT, INTERACT-2, and ATACH-2 trials demonstrated no benefit in functional outcome of aggressive antihypertensive therapy to a systolic blood pressure of less than 140 mmHg compared to a more modest goal of prevention of severe hypertension to blood pressure goals from 140 to 180 mmHg[48,51,52] for treatment of intracerebral hemorrhage. However, these studies were not specific to SAH. According to 2012 guidelines from the AHA/ASA, there is a class I recommendation for oral nimodipine to minimize poor outcome in patients with aneurysmal SAH, while other calcium channel blocking agents (oral and parenteral) have yet to be established as effective or ineffective treatment options.[30]

Hyponatremia is a common finding associated with SAH, with an incidence varying between 10-40% of cases.[53] Per 2012 AHA/ASA stroke guidelines, hypotonic fluids should be avoided.[30] Use of normal or hypertonic saline may be indicated for correction of symptomatic hyponatremia (e.g., altered mental status or seizure).

Anticoagulants can worsen the prognosis of acute SAH, and appropriate reversal is indicated. Vitamin K antagonists (e.g., Coumadin/warfarin) can be treated with vitamin K, fresh frozen plasma, and prothrombin complex concentrate.[54] In the case of bleeding in patients on aspirin, desmopressin can be a potential reversal agent. Likewise, platelet infusion can be considered when the effects of clopidogrel require reversal.[30,54] Patients on a direct oral anticoagulant should be reversed if a reversal agent is available.

Seizures are another clinical finding seen in acute SAH, but initiation of antiepileptic medications remains controversial. According to 2012 AHA/ASA stroke guidelines, there is modest evidence (class IIb, level of evidence B) to suggest utility of prophylactic anticonvulsants in the acute posthemorrhagic phase of SAH. However, data remain mixed and suggest potential harm with long-term use of antiepileptics if there is no other underlying seizure disorder.[30]

While beyond the scope of the emergency practitioner, definitive surgical management options favor endovascular coiling of intracerebral aneurysms vs. open neurosurgical clipping, although this decision should be shared between the patient and a multidisciplinary team of cerebrovascular surgeons and endo-vascular specialists.[42]

Cerebral Venous Sinus Thrombosis

Cerebral venous sinus thrombosis (CVST) is a well-described but overall less thought of entity regarding the spectrum of headache disorders. Thunderclap headache may be the main symptom in approximately 10% of patients with CVST.[55-57] Important keys to diagnosing this headache etiology partly lie with the past medical history. Similar to those with a history of deep venous thrombosis (DVT), patients who have CVST often will have a prior history of hypercoagulable disorders, pregnancy, systemic inflammatory disease, connective tissue disorders, or oral contraceptive medication use.[58,59] This is part of the reason a CVST colloquially is called a "DVT of the brain." CVST is much more prevalent in females than in males; in fact, 75% of CVST patients are female.[60] Risk factors that predispose one to CVST can be categorized generally as: infectious, hypercoagulable states, rheumatologic diseases, medications, malignancy, and other less common associations. These associations are summarized in Table 3. There are other associations that are less common (sometimes with only one case report noted), but they may be worth considering when obtaining a history and are noted at the end of Table 3.[61] Notably, there is no identifiable cause in 25% of CVST patients.[61]

CVST accounts for 50% of strokes during pregnancy and the peripartum period.[60] Indeed, it strikes more often at a younger age, being most prevalent in the second and third decades of life.[62] Almost 80% of cases occur in patients younger than 50 years of age.[63]

There are two types of CVST: those related to increased intracranial pressure attributable to impaired venous drainage, and those related to focal brain injury from venous ischemia/infarction or hemorrhage.[62] Symptoms are variable depending on the location of the

Table 3. Noted Diseases With CVST

Infectious	Intracranial infection • Abscess, subdural empyema, meningitis Regional infection • Otitis, sinusitis, orbital cellulitis, tonsillitis, dental infections, stomatitis General • Bacterial: septicemia, endocarditis, tuberculosis • Viral: measles, hepatitis, herpes simplex virus, cytomegalovirus • Parasitic: malaria, trichinosis, toxoplasmosis • Fungal: Aspergillosis, Cryptococcosis
Hypercoagulable states	Factor V Leiden Prothrombin gene mutation Protein C, S, and ATIII deficiency Homocystinuria Essential thrombocytopenia Primary polycythemia Plasminogen deficiency Heparin-induced thrombocytopenia Pregnancy
Medications	Oral contraceptives Androgens Anti-estrogen therapy Antineoplastic drugs
Malignancy	Squamous cell metastatic cervical mass Non-Hodgkin's lymphoma Bilateral glomus tumors Colorectal cancer Epidermoid carcinoma of the tongue Dysgerminoma Ewing sarcoma Paraneoplastic syndrome (rare)
Rheumatologic diseases	Behcet's disease Antiphospholipid antibody syndrome Systemic lupus erythematosus Wegener's granulomatosis Churg-Strauss syndrome
Endocrine diseases	Diabetes mellitus Hyperthyroidism
Other	Trauma Long flights Dehydration Irritable bowel disease Lumbar puncture (particularly intrathecal injection) Paroxysmal nocturnal hemoglobinuria Nephrotic syndrome Iron deficiency anemia Sickle cell anemia Renal allograft Idiopathic

Adapted from: Saadatnia M, Fatehi F, Basiri K, Mousavi SA, Mehr GK. Cerebral venous sinus thrombosis risk factors. *Int J Stroke* 2009;4:111-123.

thrombosis, but have the possibility to include headache, decreased level of consciousness, seizures, focal neurologic deficits, or even coma.[58,59] In particular, headache is present in 90% of patients, symptoms of stroke in 50%, and seizures in 40%.[58] Up to 25% of patients with CVST present with isolated headache without focal neurological findings or papilledema.[64] A D-dimer can be an important clue, as one group found that it had a sensitivity greater than 95% and negative predictive value of 99.6% when used as a test for CVST.[65] However, a follow-up study noted that this negative predictive value was formed with patients presenting with more severe symptoms, such as those with severe, resistant seizures or associated with focal signs.[66] Crassard et al found that 26% of patients had a negative D-dimer when presenting with an isolated headache. Imaging studies are needed to confirm the diagnosis.

Physical Exam/Presentation. CVST may present with varying signs and symptoms that overlap with other causes of thunderclap headache, making diagnosis particularly difficult. As always, a high clinical suspicion is required. However, emergency providers may encounter common symptoms, such as altered mental status, focal neurologic deficit, seizure, elevated intracranial pressure, or any combination of these.[60] A more complete list including less common presentations may be found in Table 4.

The 2011 Scientific Statement from the AHA/ASA includes an algorithm for workup of suspected CVST. Initially, noncontrast imaging (MRI slightly favored over CT) is performed with subsequent CT or MR venography.[62] Studies demonstrate reasonable comparability of CT/CT venography to the gold standard of intra-arterial digital subtraction angiography, with CT/CT venography having sensitivity of 95% and specificity of 91%.[67] High suspicion for CVST must guide imaging choices.

Treatment and management, much like other forms of venous thromboembolism, rely on full-dose anticoagulation with heparin or low molecular-weight heparin.[62] Recent data suggest anticoagulation is reasonable to initiate regardless of the presence of associated intracerebral hemorrhage. Patients should be admitted to a stroke unit for further evaluation, treatment, and monitoring.[62]

Pituitary Apoplexy

Pituitary apoplexy is a rare cause of headache; however, it is life-threatening. Pituitary apoplexy can manifest as a severe, abrupt-onset, thunderclap

Table 4. Presenting Symptoms of Cerebral Venous Thrombosis

Common Symptoms

- Altered mental status (encephalopathy)
- Focal deficit or seizure
- Papilledema (intracranial hypertension)
- Any combination of the above

Rare Symptoms

- Cavernous sinus syndrome
- Subarachnoid hemorrhage
- Isolated psychiatric symptoms
- Isolated or multiple nerve palsies
- Transient ischemic attacks
- Tinnitus
- Attacks of migraine with aura
- Isolated headache
- Thunderclap headache

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headache; in fact, it is known as one of the causes of non-aneurysmal SAH.[11] Apoplexy refers to a constellation of symptoms characterized by sudden onset of severe headache, visual impairment, vomiting, ophthalmoplegia, and altered level of consciousness.[68] Common comorbidities were reported to be hypertension (39%), dyslipidemia (34.5%), and obesity (27.5%).[68] Less commonly, patients had diabetes mellitus (12.6%), with up to one-fourth of patients being previous smokers.[68]

Pituitary apoplexy typically occurs in the setting of a spontaneous hemorrhage or infarction of a pre-existing pituitary adenoma.[2] Once hemorrhage or ischemia occurs, rapid expansion of a pituitary adenoma can cause pituitary apoplexy in about 14-22% of patients.[69] Given involvement of the pituitary gland, hormonal effects can occur acutely after the event or have a delayed presentation. Hypopituitarism ccurs in 70-80% of patients with pituitary apoplexy.[69] Headache along with visual symptoms are possible. In 43% of cases, involvement of multiple cranial nerves has been described.[69]

Physical Exam/Presentation. In one study, the most common presenting symptom was a sudden severe headache that was described as frontal or retro-orbital.[68] Approximately half of patients had visual abnormalities in combination with their headache, with blurred vision being the most common complaint in 20% of patients.[68] As mentioned above, multiple cranial nerve palsies are common, with unilateral CN III palsy seen in about two-thirds of patients. Visual field deficits were seen in a third of cases, with bitemporal hemianopsia seen in almost 60% of patients. Facial weakness also was seen in 62% of patients.

A rare diagnosis, up to 80% of cases of pituitary apoplexy initially may be misdiagnosed as a more common neurological condition.[70] The Society for Endocrinology published pituitary apoplexy emergency guidance guidelines in 2016, with initial management emphasizing hemodynamic stability and appropriate correction of electrolyte abnormalities or fluid imbalance.[70] MRI is the imaging modality of choice, confirming the diagnosis of pituitary apoplexy in 90% of cases.[70] However, a dedicated pituitary CT may be performed if there are contraindications to MRI.[70]

Beyond baseline laboratory studies (such as blood counts, electrolytes, and coagulation studies), serologic analysis of pituitary hormones (e.g., IGF1, GH, PRL, TSH, T4, LH, FSH, cortisol, testosterone, or estradiol) may guide therapies.[70] Consultation with neurosurgical and endocrinology services is appropriate when the diagnosis of pituitary apoplexy is established. Admission to a neurosurgical critical care unit is indicated after initial stabilization and resuscitation.

Ischemic Stroke

The majority of thunderclap headaches are described in the setting of bleeding or vascular disorders that are able to cause a rise in intracranial pressure. Although seemingly inconsistent thunderclap headaches have been described in patients with ischemic strokes. A large retrospective study of 2,196 patients demonstrated that 27% of patients experienced headache at stroke onset.[71] Headache was found to be bilateral in 61% of patients, with unilateral headache in the remainder. It should be noted, however, that the quality of the headache — specifically, whether it was thunderclap in nature — was not discussed by the authors.[71] Notably, patients with unilateral headache were found to have their lesion located on the ipsilateral side.[71,72]

The frequency of headaches depends on various factors, including size, location, duration of ischemia, history of migraine, age, and genetic background.[6,73] Younger patients, as well as females and those with diabetes, seem to present more commonly with headache.[71,72] Although migraine previously was not considered a risk factor for headache associated with stroke, Tentschert et al reported that patients with a history of migraine had a 1.7-fold risk of developing headache with stroke.[71] One study noted that headache was not linked to risk factors such as hypertension or heart disease.[72]

However, most patients with ischemic strokes do not present with thunderclap headache.[6] According to Matharu et al, three patients have been reported in the literature as having thunderclap headache, along with one case in which thunderclap headache was the primary clinical feature of embolic bilateral cerebellar infarcts.[4,6,74] Ischemic strokes may be relatively straightforward to distinguish from other causes of thunderclap headache, given the accompanying focal neurologic deficits and historical findings. Regardless, one should recognize the potential, although rare, for ischemic strokes to present with thunderclap headache.

Physical Exam/Presentation. As mentioned above, a stroke typically is suspected based on the patient's neurologic deficits. Headache may be accompanied by ischemic stroke onset in up to 34% of patients.[72] However, that study did not assess the quality of the headache. Another study noted that the severity of headache showed no relation to size or lesion localization.[75]

Stroke diagnosis requires rapid assessment of hemorrhagic vs. ischemic etiology with CT and MRI, and management is guided by chronicity and

duration of symptoms. Timely admission or transfer to a qualified stroke center is appropriate in the acute setting to prevent worsening ischemia or infarction.[76,77] Depending on inclusion and exclusion criteria per the National Institute for Neurologic Disorders and Stroke, 2013 joint guidelines published by ACEP and the American Academy of Neurology (AAN) give a level A recommendation for offering tissue plasminogen activator (tPA) as treatment for acute ischemic stroke within three hours of symptom onset.[29,76] However, in 2015 this recommendation was changed to level B and stressed that tPA should be considered, suggesting that shared decision-making with the patient and his or her family should be attempted.[78] The 2013 ACEP/AAN guidelines give a level B recommendation for tPA within 4.5 hours of acute ischemic stroke symptom onset if inclusion/exclusion criteria of the European Cooperative Acute Stroke Study (ECASS) III are met; the caveat is that tPA usage within the three- to 4.5-hour timeframe is off-label and outside of the three-hour window currently set by the U.S. Food and Drug Administration (FDA).[29,76] Patient-centered, shared decision-making techniques and a multidisciplinary approach should be used to educate the patient on the risks and benefits of tPA therapy for acute ischemic stroke.[79]

Cervical Artery Dissection

Among the many vascular causes of headache, arterial dissection remains high on the list for emergency practitioners given its associated morbidity and mortality if missed. Thunderclap headache is described in 13% and 22% of patients with carotid and vertebral dissection, respectively.[6,80] Generally, dissections will present with focal neurologic deficits, and the causative vessel will determine the associated symptomatology. Often times, there can be a delay in neurologic symptoms from later thrombosis of the dissected segment, causing obstruction of flow or embolization of thrombus from the dissected segment to the intracranial arteries.[81]

In general, cervical artery dissection is an uncommon disease with a mean age of occurrence of 44 years. After age 65, the disease becomes increas-ingly rare.[82] Heritable diseases such as Ehlers-Danlos, Marfan syndrome, polycystic kidney disease, and osteogenesis imperfecta have been implicated.[82,83] Only 1-2% of all ischemic strokes are caused by cervical artery dissection, but in younger patients, cervical artery dissection accounts for 10-25% of strokes.[84] Dissections are more common in the carotid artery than the vertebral artery.[82] Overall, cervical artery dissection has been well studied with multiple risk factors delineated. Environmental factors were most commonly found to be various degrees of trauma, such as a motor vehicle collision with rapid deceleration and a hyperflexion injury. As may be expected, the risk of cervical artery dissection increases with facial fractures, traumatic brain injury, and skull base fractures.[83] Other mechanisms of injury may lead to hyperextension, rotation, lateroversion, or compression, such as in strangulation. One must maintain a high level of suspicion for dissection when evaluating neck-related injuries that present with a headache.

Dissection is associated with intrinsic factors such as fibromuscular dysplasia, aortic-root dilation, and bicuspid aortic valve. Unlike in SAH, family history is not a common risk factor for this process.[84]

Cervical neck pain is twice as common in patients with vertebral artery dissection compared to those with internal carotid dissection.[84] Commonly known symptoms of carotid artery dissection include those attributed to a partial Horner's syndrome, namely miosis and ptosis; however, this only occurs in about 25% of patients.[2] In contrast, vertebral artery dissections typically will have vertigo as a presenting symptom, along with headache and neck pain, commonly in the setting of trauma.[2] Patients typically have headaches, facial pain, or neck pain that usually is ipsilateral to the dissected vessel and sudden in onset.[11,84] A clear history and thorough neurologic examination can assist when differentiating these causes of headache.

Physical Exam/Presentation. Dissection patients will present most commonly with headache, neck pain, and facial pain. Up to 69% of patients will present with a headache; however, the majority of these will be gradual in onset.[83] According to study by Silbert et al, the incidence of thunderclap headache in internal carotid dissection vs. vertebral artery dissection was 14% to 22%, respectively.[80] The location of the headache also tends to be unilateral in the frontal or frontoparietal region.[80,85] Other associated symptoms include facial pain, neck pain, cranial nerve palsies, and pulsatile tinnitus.[83]

Current data are limited and controversial regarding medical management of cervical artery dissection, which can be diagnosed with CT angiography.[83] While treatment of a vascular dissection with anticoagulant or antiplatelet agents may seem dangerous, anticoagulation is initiated to minimize clot burden and prevent the cerebral embolization of clots, which can cause stroke.[86] Propagation of cervical artery dissection can spread intracranially, causing SAH. Patients with cervical artery dissection require vascular surgery consultation with surgical or endovascular management. Similar to ischemic stroke, tPA may be indicated if there are no contraindications and the dissection has not spread intracranially or does not involve the aorta.[86]

Hypertensive Crisis

It is a relatively common assumption that acute blood pressure elevation is linked directly to headaches among patients who present to the ED, but hypertensive headache presenting as thunderclap headache is rare. Studies have shown that mild blood pressure elevation is not linked to acute headache. In fact, a study by Gus et al that monitored ambulatory blood pressure and relation to headache found that blood pressure did not differ significantly between hypertensive patients with and without headache during 24-hour ambulatory blood pressure monitoring.[87]

However, severe elevation or rapid increase in blood pressure can be related to headache, such as in pheochromocytoma or posterior reversible encephalopathy.[2] About 20% of patients with hypertensive crisis have associated headaches, but most of these headaches are not thunderclap headache.[6,88]

According to the International Headache Society, headache caused by increases in intracranial pressures have been well described.[11] It has been suggested that the head pain associated with acute hypertensive crises can be the direct result of increased pressure stimulating the sensory afferents that innervate the larger intracranial arteries.[6,89] The paucity of studies evaluating headache severity and association with quantitative blood pressure readings makes drawing conclusions about the relationship to thunderclap headache difficult; however, it has been shown that most headaches attributed to severe hypertension do have readings in the range of 250/150 mmHg.[90] Additional studies are warranted to investigate this relationship further.

Physical Exam/Presentation. An acute hypertensive crisis may not present reliably with specific symptoms; instead there are disease processes or constellations of findings that may be encountered. Hypertensive crises may present as hypertensive encephalopathy, acute aortic dissection, acute pulmonary edema, acute myocardial infarction, eclampsia, acute renal failure, and microangiopathic edema.[91] It is important to note that the absolute number of the blood pressure reading is not as important as the rate of increase. Fundoscopic exam commonly reveals advanced retinopathy, hemorrhages, exudates, as well as papilledema, in patients with hypertensive encephalopathy.[91]

Although hypertension is a commonly encountered vital sign abnormality in the ED, emergent lowering of elevated blood pressure is only indicated for hypertensive emergencies with evidence of acute end organ dysfunction.[91,92] The goal of treatment for a true acute hypertensive emergency is to reduce the mean arterial pressure by at least 10-15% but no more than 25% within one hour of presentation.[92-94]

Numerous antihypertensive agents can be considered. However, in the case of a hypertensive emergency, relatively shorter-acting intravenous agents are preferred over slower-onset oral agents. Commonly recommended agents for treatment of a hypertensive emergency include esmolol, labetalol, fenoldopam, nitroprusside, and nicardipine.[92] Agents to avoid include nitroglycerin, hydralazine, and diuretics.[92] Nitroglycerin acts primarily as a venodilator, and only acts on arterial hypertension at high doses with risk of hypotension and reflex tachycardia. Hydralazine's long-acting and often unpredictable pharmacology make it less useful in treatment of hypertensive emergencies; and diuretics can cause a precipitous drop in blood pressure leading to cerebral ischemia and stroke in patients who already may be intravascularly depleted.[92] Admission to an intensive care unit for further monitoring and titration of antihypertensive therapy is appropriate.[91]

Reversible Cerebral Vasoconstriction Syndrome

Reversible cerebral vasoconstriction syndrome (RCVS) is a well-studied, but poorly understood, condition that can present as thunderclap headache. Among many other described headache disorders, RCVS is a rare cause of thunderclap headache. RCVS is not one specific entity, but rather a term that covers a group of recurrent headache syndromes to include Call-Fleming syndrome, thunderclap headache with reversible vasospasm, benign angiopathy of the central nervous system, and postpartum cerebral angiopathy, among others.[95,96] As the name implies, RCVS presents as recurrent attacks and episodes of vasoconstriction. Imaging findings may or may not show vasoconstriction depending on when the images are taken. Given these episodes of described vasoconstriction, exposure to vasoactive substances is a risk factor for this condition, along with postpartum state.[11]

Patients typically present in the fifth decade of life,[97-99] with women more commonly affected. Depending on the study, vasoactive substances have been found as precipitant causes in up to 52% of cases, according to one prospective trial of 89 patients at a single institution.[97] Some medications implicated include sumatriptans, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, pseudoephedrine in cough suppressants, amphetamines, cocaine, and marijuana.[99] Recurrent thunderclap headaches are common in this disease, occurring within one to four weeks, may help with distinguishing this malady from others. The frequency and intensity of thunderclap headache may diminish over time.[99]

Clinically, RCVS can present with focal neurologic deficits and seizure activity, in contrast to other benign thunderclap headache disorders.[95] Most patients have multiple thunderclap headaches that can recur every day for a few days to four weeks.[3,100,101] There are certain diagnostic criteria, according to the ICHD, which include the following: headache with or without focal deficits and/or seizures with recurrence of headache over a period of one month, thunderclap onset, triggered by sexual activity, exertion, Valsalva maneuvers, emotion, bathing/showering, no new significant headache occurring more than one month after onset, and SAH must be excluded as a cause.[11] In general, RCVS may account for some unidentified causes of thunderclap headache and should be considered only when more emergent etiology has been evaluated. The emergency physician should have a high suspicion for this disorder when a patient presents with multiple episodes of thunderclap headache, especially within several weeks.

Physical Exam/Presentation. Headache is the most common symptom — and the only reliable symptom — in patients presenting with RCVS.[97-99] Focal neurologic deficits have been documented in more than 40% of cases,[99] with seizures present in up to 17%. Some neurologic findings seen in up to one-third of patients include those that may be seen with a transient ischemic attack, such as aphasia, hemiparesis, or ataxia.[99] These deficits can last anywhere from minutes to four hours and are more commonly of sudden onset.[97] Persistent symptoms should warrant a workup for stroke. Physical exam findings may not always be present and cannot be relied on for diagnosis. Notably, up to about half of patients will present with an elevation in blood pressure.[98]

Diagnosis/Treatment/Management. There are no specific diagnostic criteria for the identification of RCVS. However, clinical history in addition to angiographic evidence of multifocal

Table 5. Diagnostic Criteria for Spontaneous Intracranial Hypotension Causing Headache

A. Any headache fulfilling criterion C
B. Low cerebrospinal fluid pressure (< 60 mm CSF) and/or evidence of cerebrospinal fluid leakage on imaging
C. Headache has developed in temporal relation to the low cerebrospinal fluid pressure or cerebrospinal fluid leakage, or has led to its discovery
D. Not better accounted for by another ICHD-3 diagnosis

segmental cerebral artery vasoconstriction (whether via traditional invasive angiography or by indirect MR angiography or CT angiography) that disappear within 12 weeks support the diagnosis of RCVS.[96,101] Imaging demonstrates a "beading" appearance of cerebral arteries due to intermittent constriction and dilation along vascular channels.[96]

There are no randomized clinical trials favoring any one treatment regimen. To date, the literature describing management of RCVS is limited to expert opinion and observational data.[96,101] Proposed therapies include avoidance of triggers (such as physical exertion, sexual activity, or Valsalva maneuver), calcium channel blockers, glucocorticoids, and observation.[101]

Nonvascular Causes

Spontaneous Intracranial Hypotension

Spontaneous intracranial hypotension (SIH) is related to low levels of cerebral spinal fluid (CSF), as a direct result of leaks located in the vertebral column or skull.[102-104] Rarely, this can manifest as a sudden onset headache, only affecting an estimated 5/100,000 patients.[102] This type of headache is more commonly associated with recent dural penetration, either during LP, epidural anesthesia, or any operative procedure that involves opening the dura.[2] According to the ICHD, if iatrogenic (dural puncture within one month), this headache is no longer classified as SIH.[11] SIH typically is preceded by minor trauma, such as falls, lifting, coughing, and sports activities.[6]

Clinically, the headache is described as positional and is exacerbated by upright posture and improved lying down.[6] The headache typically is relieved in the recumbent position within 15-30 minutes.[105] SIH also can mimic other more serious causes of headache, namely SAH, and approximately 15% of patients with SIH will present with thunderclap headache.[6,106] The postural nature of this headache can be a helpful distinguishing factor compared to those who present with SAH and prefer to lie flat.[3] The symptoms and time course of this disease can be quite debilitating, and patients who have SIH can be incapacitated for years and find difficulty engaging in any useful activity while upright.[102] Although patients with this disorder may not present to the ED often, unnecessary testing and treatment are possible. Diagnosing SIH early can lead to treatment with a high success rate and near immediate relief for the patient.[102,107,108]

Physical Exam/Presentation. As mentioned above, up to 15% of patients with SIH will present with thunderclap headache. Apart from an orthostatic headache, common symptoms include neck stiffness, nausea, vomiting, tinnitus, auditory muffling, horizontal diplopia, blurry vision, interscapular pain, and low back pain.[55]

The IHS notes that the headache typically is accompanied by neck stiffness and subjective hearing symptoms, and will remit with normalization of pressure. There may be improvement when the patient is lying down; however, symp-toms may not resolve immediately and may last hours. Less common symptoms include ataxia, subdural hematoma, and coma, among others.[55] There is a report of a patient with intracranial hypotension presenting with frontotemporal dementia.[109]

Diagnosis/Treatment/Management. The IHS has revised the criteria for the diagnosis of SIH, which are summarized in Table 5. Treatment evidence for SIH is limited. Case studies report successful treatment by positioning the patient in the Trendelenberg position[110] or by placing a cervical epidural blood patch for cerebrospinal fluid leak.[111] A small observational study noted an 8.5% post-procedural incidence of epidural blood patch spread to the subarachnoid space on CT. This caused no significant neu-rologic outcomes or change in thera-peutic efficacy.[112] Further case reports suggest roles for steroids or occipital nerve blocks.[113,114]

Retroclival Hematoma

Retroclival hematoma is another lesser known condition with the potential to present with thunderclap headache. The literature describes this entity as a rare manifestation of severe head and neck injuries in which there is atlantoaxial dislocation.[6,115,116] It is more commonly associated with the pediatric population, given the anatomical differences at the craniocervical junction compared to adults.[117] Although mainly reported as post-traumatic, a recent case series by Narvid et al described patients with spontaneous retroclival hematoma, most of which were associated with concurrent intraventricular hemorrhage.[118]

Both retroclival epidural hematomas and retroclival subdural hematomas have been reported, and the anatomical location of these hematomas is an important distinction to make. Retroclival epidural hematomas are restricted by the boundaries of the tentorial membrane, which is attached inferiorly to the axis and superiorly to the occipital bone along the clivus. In contrast, retroclival subdural hematomas are not restricted and can disseminate from the intracranial to the spinal subdural space.[117,119] This becomes important regarding the appropriate diagnostic workup, which inevitably will include CSF analysis and imaging studies.

A recent retrospective review of patients with MRI evidence of pituitary apoplexy showed that retroclival expansion occurred in 56% of cases, whereas

Table 6. Presenting Signs and Symptoms of Colloid Cyst of the Third Ventricle

Headache (68-100%)
Drop attacks (4-21%)
Cognitive status change (21-22%)
Vomiting (37-57%)
Loss of consciousness (13-28%)
Papilledema (47-72%)

Adapted from: Young WB, Silberstein SD. Paroxysmal headache caused by colloid cyst of the third ventricle: Case report and review of the literature. *Headache* 1997;37:15-20.

there were only two prior case reports.[120] Although rare, one should have an increased suspicion for retroclival hematoma in the pediatric population, post-traumatic patients, and those with concomitant pituitary apoplexy.

Physical Exam/Presentation. In trauma patients, the most common mechanism is a hyperflexion or hyperextension injury to the neck. This type of injury can lead to soft tissue injury or fractures causing a retroclival hematoma.[117] There is a significant number of cases in children linking retroclival hematoma to motor vehicle collision. Cases of abuse in children also have revealed retroclival hematomas. Many of these patients will present with depressed GCS score, attributed to their initial traumatic injury. In adults, physical signs may include isolated cranial nerve palsies, either unilateral or bilateral.[117] Ophthalmoplegia, hypoacusis, visual field deficits, and even hemiparesis have been encountered.[117] The most commonly involved nerve is the sixth cranial nerve, with unilateral and bilateral involvement reported.[117]

Management. Given the rarity of retroclival hemorrhage, studies regarding management are limited to case reports and modest case series.[118] The prognosis varies, but is often excellent with supportive and close/intensive observational management.[118] Concerning features, such as hydrocephalus, atlantoaxial instability, and brainstem compression, require acute neurosurgical intervention and portend worsening outcome.[118] Noninvasive angiographic MR and CT imaging studies with evaluation for underlying coagulopathy were standard procedure for evaluation of spontaneous retroclival hematoma over a three-year observational period in one small (i.e., n = 4) case series.[118] The case series suggests close monitoring is required in the acute setting. With nonoperative management and supportive care, none of the enrolled patients were found to have focal neurologic findings on 90-day outpatient follow-up, and only one patient described mild intermittent headaches.[117,121]

Colloid Cyst of the Third Ventricle

Colloid cysts of the third ventricle can cause sudden onset headache secondary to sudden obstruction of normal CSF flow. The risk of obstructive hydrocephalus begins at a cyst diameter of 7 mm measured on axial T1-weighted MRI.[122] The location of these lesions in various regions of the foramen of Monro makes acute obstruction of CSF flow more likely.[122] This headache may start abruptly and may last for seconds to a day, with rapid resolution of pain.[6] Aside from headache, patients can present with symptoms similar to those of hydrocephalus, including loss of consciousness, cognitive changes, seizures, coma, and death. Nausea and vomiting are reported in approximately 50% of cases.[55,123]

In some patients, the headache can be relieved in the recumbent position.[55] While the disease does have the ability to cause rapid clinical deterioration, it is an uncommon entity. Previous reviews indicated that these cysts accounted for approximately 0.5% of intracranial tumors;[123] but a recent review by Beaumont et al showed an incidence of 3.2 per million per year, which accounts for approximately 2% of all intracranial tumors.[122]

Physical Exam/Presentation. In a case series of 29 patients, seven people presented with acute onset of headache.[124] This case series also reported that after headache, the most common presenting symptom was sudden weakness of the lower limbs, causing falling without loss of consciousness. As summarized in Table 6, the most common presenting signs and symptoms are headache and papilledema, according to a case series review.[123]

Treatment/Management. Patients with colloid cysts of the third ventricle should be managed in consultation with a qualified neurosurgeon. Acutely symptomatic patients may require emergent — and risky — operative interventions.[125,126]

Agrawal et al enumerate the perils of surgical cyst resection: midline location, anatomic depth, infection risk, obstructive hydrocephalus, and sudden death, among others.[125] Despite these potential pitfalls, early diagnosis and complete resection are associated with good neurological outcomes.[125]

Horn and Feiz-Erfan described the findings of a decade-long retrospective analysis of 55 patients treated operatively — 28 endoscopic cases and 27 via open microsurgical transcallosal craniotomy.[126] Equivalent neurological outcomes and number of complications requiring reoperation were observed between the two groups.[126] The open approach was noted to have more infec-tion-related complications; a higher number of (open) reoperations were reported in the endoscopic cohort.[126]

Primary Thunderclap Headache

Primary thunderclap headache is a diagnosis of exclusion. This headache is a benign headache and similar in presentation to more serious, secondary causes of thunderclap headache. One must exhaust all possibilities of thunderclap headache prior to making a diagnosis of primary thunderclap head-ache, which includes negative diagnostic testing. Classification criteria exist for this headache via the ICHD, which state that the headache must be severe, sudden onset, reach maximum intensity within a minute, and endure from one hour to 10 days.[11,55] Although classified as a separate entity according to the ICHD, there is likely overlap, and pri-mary thunderclap headache may exist as the same entity as other described headaches, including benign sexual headache, migrainous vasospasm, benign vascular headache, etc.[55] There is still debate as to whether primary thunderclap headache even exists.[3]

Post-coital, Exertional, and Cough Headaches

Among the primary headache disorders described by the ICHD, post-coital, exertional, and cough headaches have been associated with thunderclap headache. These headaches should be considered once more serious, secondary causes of headache have been ruled out. The historical findings become paramount when considering these diagnoses. Concerning sexual headaches (post-coital headaches), the ICHD requires that the headache must be brought on by and occur only during sexual activity, with pain increasing in intensity with sexual excitement and/or abrupt, explosive intensity just before or with orgasm.[11] Three subtypes have been described previously, including the "dull" type, "explosive" type, and "postural" type.[127] A patient may experience a dull, gradual pain that increases with sexual excitement, or explosive type with abrupt headache at the moment of orgasm, with the latter being the most common type (about 70%).[127] Previous criteria in ICHD-I and ICHD-II described two subforms of this headache, pre-orgasmic and orgasmic; however, clinical studies have been unable to distinguish between these subforms, and headache associated with sexual activity is now regarded as a single entity with variable presentation.[11] Sexual headache is classified as its own primary headache disorder, but interestingly, a prospective series showed that 60% of patients with isolated sexual headaches had RCVS.[3,128] This is important to consider, as these two causes may be difficult to distinguish.

Another important primary headache disorder to consider with regard to thunderclap headache is primary exertional (exercise) headache. According to the ICHD, this headache must be brought on by and occur only during or after strenuous physical exercise and should last less than 48 hours.[11] The mechanism underlying this headache disorder is unknown; however, most investigators believe that these headaches are vascular in origin, hypothesizing that a venous or an arterial distension secondary to physical exercise is the pain-inducing mechanism.[127,129,130] In connection with a large-scale study of headache epidemiology in Norway, the prevalence of exertional headache was 12.3%.[131] According to Sjaastad et al, exertional headache seems to coexist with migraine in 56% of cases.[131] There is no clear definition in the literature as to what constitutes "exertion" with relation to this headache, and it can be assumed that physically strenuous exercise may differ among individuals.

A similar headache that can be precipitated by short bursts of strain-like activity is the primary cough headache. In contrast to sustained, physically strenuous exertional headaches, primary cough headache is brought on only in association with coughing, straining, and/or other Valsalva maneuver.[11] These headaches are described as sudden onset — lasting only between one second and two hours — in contrast to exertional headaches, which can persist up to 48 hours.[11] This headache is described by the ICHD as a benign headache disorder; however, type I Chiari malformation frequently has been associated with primary cough headache.[127,132,133] These headaches are fairly easy to distinguish, provided the correct clinical context, but it is paramount, as stated previously, that these primary headache disorders only be considered once secondary causes have been evaluated thoroughly.

Physical Exam/Presentation/Management. Patients presenting to the ED with sexually related headache have an average age in the mid to late 30s.[134,135] The same study also noted that the majority of their patients had an explosive-type headache, which was either bilateral and diffuse, or occipital.[134] Dull, throbbing, and stabbing were equally as common.[134] These headaches may recur months or years later.[135] Propranolol and indomethacin have been suggested as useful prophylaxis in cases of chronic coital cephalgia and cough-induced headache.[134]

Summary

Sudden onset headache, or thunderclap headache, is a concerning presentation in the ED. It traditionally is defined as a headache that reaches peak intensity within one minute; however, landmark studies evaluating the accuracy of workup for SAH have used one hour as the cutoff time for defining sudden onset, and providers should consider this when evaluating their patients in the ED. Furthermore, there are many headache types in addition to SAH that can present with sudden onset headache. Some of these headaches, while rarer, can be very dangerous. A thorough history followed by a focused physical exam is the cornerstone of evaluating patients with sudden-onset headache. Management of these patients can vary widely depending on the disease. Providers need to keep a wary eye on these patients, as often times, they have conditions that are deadly.

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CME/CE Questions

1. What is the classic definition of a thunderclap headache in terms of when the headache has to reach maximal intensity?
   a. Within one minute
   b. Within two hours
   c. Within six hours
   d. Within 24 hours
   e. No specific time limit, just as long as the patient says sudden instead of gradual
2. Which of the following must be present to consider subarachnoid hemorrhage?
   a. Meningismus
   b. Photophobia
   c. Altered mental status
   d. None of the above
3. The American College of Emergency Physicians recommends which of the following strategies for working up subarachnoid hemorrhage?
   a. Computed tomography (CT) only within six hours, and CT followed by lumbar puncture (LP) after six hours
   b. CT followed by LP regardless of time passed since onset of symptoms
   c. CT followed by computed tomography angiography (CTA) regardless of time passed since onset of symptoms
   d. Shared decision-making with the patient regarding CT only vs. CT/LP vs. CT/CTA
4. Which of the following lab values is sensitive for cerebral venous sinus thrombosis?
   a. S100 calcium-binding protein B (S100B)
   b. Glial fibrillary acidic protein (GFAP)
   c. D-dimer
   d. Matrix metallopeptidase 9 (MMP-9)
   e. Troponin
5. A patient presents with a thunderclap headache that started when she was having intercourse. It lasted 30 minutes and now is gone. The examination is normal. What is the correct treatment plan for this patient?
   a. CT, and if negative, LP
   b. CT, and if negative, CTA
   c. MRI
   d. Reassurance
6. Which of the following is *not* a risk factor for cerebral venous sinus thrombosis?
   a. Male gender
   b. History of deep vein thrombosis
   c. Malignancy
   d. Young adult
7. A patient presents with an acute onset of neck pain and vertigo after a car accident. CT of the head and neck are normal. Which of the following disorders should be considered?
   a. Subarachnoid hemorrhage
   b. Vertebral dissection
   c. Post-exertional headache
   d. Pontine hemorrhage

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EMERGENCY MEDICINE REPORTS

Sudden Onset Headache

Key Clinical Features of Vascular and Nonvascular Causes of Thunderclap Headache

Vascular Causes	Characteristics
Subarachnoid hemorrhage	Neck stiffness, neurologic signs, altered level of consciousness
Cerebral venous sinus thrombosis	Female to male predominance; can present with focal neurologic deficits and seizures
Pituitary apoplexy	Associated with known pituitary adenoma; can have visual symptoms and cranial nerve deficits
Ischemic stroke	Uncommon, presents with focal neurologic deficits
Cervicocephalic arterial dissection	Can present with Horner's syndrome
Acute hypertensive crisis	Extreme blood pressure elevations, signs of end organ damage
Reversible cerebral vasoconstriction syndrome	Recurrence of thunderclap headache
Nonvascular Causes	**Characteristics**
Retroclival hematoma	Pediatric predominant; precipitated by minor trauma; associated with atlantoaxial dislocation
Colloid cyst of the third ventricle (post fossa mass)	Can be associated with other symptoms of obstructive hydrocephalus (i.e., gait ataxia, confusion)
Primary thunderclap headache	Indistinguishable from secondary causes; diagnosis of exclusion
Post-coital headache	Explosive headache occurring just before or during orgasm
Exertional headache	Associated with sustained physical exertion, lasts < 48 hours
Primary cough headache	Brief, associated with straining maneuvers (i.e., Valsalva, cough); Chiari malformation associated
Spontaneous intracranial hypotension	Postural; worse with standing and improved with supine position

Differential Diagnosis

Vascular Related Causes

- Subarachnoid hemorrhage
- Cerebral venous sinus thrombosis
- Pituitary apoplexy
- Ischemic stroke
- Cervical artery dissection
- Acute hypertensive crisis
- Reversible cerebral vasoconstriction syndrome

Nonvascular Related Causes

- Spontaneous intracranial hypotension
- Retroclival hematoma
- Colloid cyst of the third ventricle
- Primary thunderclap headache
- Post-coital headache/exertional headache/primary cough headache

Presenting Symptoms of Cerebral Venous Thrombosis

Common Symptoms

- Altered mental status (encephalopathy)
- Focal deficit or seizure
- Papilledema (intracranial hypertension)
- Any combination of the above

Rare Symptoms

- Cavernous sinus syndrome
- Subarachnoid hemorrhage
- Isolated psychiatric symptoms
- Isolated or multiple nerve palsies
- Transient ischemic attacks
- Tinnitus
- Attacks of migraine with aura
- Isolated headache
- Thunderclap headache

Noted Diseases With CVST

Infectious	Intracranial infection • Abscess, subdural empyema, meningitis Regional infection • Otitis, sinusitis, orbital cellulitis, tonsillitis, dental infections, stomatitis General • Bacterial: septicemia, endocarditis, tuberculosis • Viral: measles, hepatitis, herpes simplex virus, cytomegalovirus • Parasitic: malaria, trichinosis, toxoplasmosis • Fungal: Aspergillosis, Cryptococcosis
Hypercoagulable states	Factor V Leiden Prothrombin gene mutation Protein C, S, and ATIII deficiency Homocystinuria Essential thrombocytopenia Primary polycythemia Plasminogen deficiency Heparin-induced thrombocytopenia Pregnancy
Medications	Oral contraceptives Androgens Anti-estrogen therapy Antineoplastic drugs
Malignancy	Squamous cell metastatic cervical mass Non-Hodgkin's lymphoma Bilateral glomus tumors Colorectal cancer Epidermoid carcinoma of the tongue Dysgerminoma Ewing sarcoma Paraneoplastic syndrome (rare)
Rheumatologic diseases	Behcet's disease Antiphospholipid antibody syndrome Systemic lupus erythematosus Wegener's granulomatosis Churg-Strauss syndrome
Endocrine diseases	Diabetes mellitus Hyperthyroidism
Other	Trauma Long flights Dehydration Irritable bowel disease Lumbar puncture (particularly intrathecal injection) Paroxysmal nocturnal hemoglobinuria Nephrotic syndrome Iron deficiency anemia Sickle cell anemia Renal allograft Idiopathic
Adapted from: Saadatnia M, Fatehi F, Basiri K, Mousavi SA, Mehr GK. Cerebral venous sinus thrombosis risk factors. *Int J Stroke* 2009;4:111-123.	

Diagnostic Criteria for Spontaneous Intracranial Hypotension Causing Headache

A. Any headache fulfilling criterion C
B. Low cerebrospinal fluid pressure (< 60 mm CSF) and/or evidence of cerebrospinal fluid leakage on imaging
C. Headache has developed in temporal relation to the low cerebrospinal fluid pressure or cerebrospinal fluid leakage, or has led to its discovery
D. Not better accounted for by another ICHD-3 diagnosis

Presenting Signs and Symptoms of Colloid Cyst of the Third Ventricle

Headache (68-100%)
Drop attacks (4-21%)
Cognitive status change (21-22%)
Vomiting (37-57%)
Loss of consciousness (13-28%)
Papilledema (47-72%)

Adapted from: Young WB, Silberstein SD. Paroxysmal headache caused by colloid cyst of the third ventricle: Case report and review of the literature. *Headache* 1997;37:15-20.

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