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Abrupt-Onset Severe Headaches

Yo-El S. Ju, M.D.[1] and **Todd J. Schwedt, M.D.**[1]
[1]Department of Neurology, Washington University School of Medicine, St. Louis, Missouri

Abstract

Thunderclap headache, a severe headache which is maximal in intensity at onset, is associated with numerous underlying disorders, including subarachnoid hemorrhage, unruptured intracranial aneurysm, cervical artery dissection, cerebral venous sinus thrombosis, stroke, intracranial hemorrhage, reversible cerebral vasoconstriction syndrome, and reversible posterior leukoencephalopathy. After exclusion of all possible causes, thunderclap headache may be considered a primary headache. This review summarizes the diagnostic considerations and clinical approach to thunderclap headache, with particular emphasis on the reversible cerebral vasoconstriction syndromes.

Keywords

Thunderclap headache; subarachnoid hemorrhage; sentinel headache; reversible cerebral vasoconstriction syndromes

Thunderclap headache (TCH) is defined as a severe headache reaching maximal intensity within seconds to a minute.[1] The phrase “worst headache of my life” is often used interchangeably, although this phrase ignores the most distinguishing feature of TCH, which is its rapid onset. Initially, TCH was reported as the “sentinel headache” of unruptured intracranial aneurysm.[2] However, numerous etiologies of TCH, ranging from benign to life-threatening, have now been recognized. Most notably, aneurysmal subarachnoid hemorrhage (SAH) classically presents with TCH. Thus, TCH is approached as a neurologic emergency. TCH has also been associated with unruptured intracranial aneurysms (“sentinel headache”), cerebral artery dissection, cerebral venous sinus thrombosis, stroke, intraparenchymal hemorrhage, intracranial infection, spontaneous intracranial hypotension, and the reversible cerebral vasoconstriction syndromes (Table 1). Reversible cerebral vasoconstriction syndrome is a term that unifies several previously described etiologies of TCH associated with reversible intracranial vasoconstriction. This includes Call–Fleming syndrome, benign angiopathy of the central nervous system, situational or drug-related TCH, postpartum angiopathy, and others. In this review, we discuss presumed causes of TCH and a prudent approach to the evaluation of the patient with TCH.

SUBARACHNOID HEMORRHAGE AND SENTINEL HEADACHE

Thunderclap headache is the classic presenting symptom of aneurysmal subarachnoid hemorrhage. Subarachnoid hemorrhage is present in ~25% of patients with TCH, and 50% of patients with SAH present with TCH without other symptoms.[3] It is unknown whether

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Address for correspondence and reprint requests: Todd J. Schwedt, M.D., Assistant Professor of Neurology and Anesthesiology, Washington University School of Medicine, 660 South Euclid Avenue, Box 8111, St. Louis, MO 63110 schwedtt@neuro.wustl.edu.

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aneurysmal SAH causes pain by rapid stretching of the vessel wall, irritation from blood products in the subarachnoid space, elevation in intracranial pressure, or other effects. Most cases of SAH are easily diagnosed by noncontrast brain computed tomography (CT) showing acute blood in the subarachnoid space. Cerebrospinal fluid (CSF) evaluation is used to diagnose the small percentage of cases that are not detected via brain CT. Given the high morbidity and mortality associated with SAH, all patients with TCH should be urgently evaluated for SAH. Patients with aneurysmal SAH, even those without additional neurologic deficits on initial presentation, are at high risk for rebleeding and acute decompensation. Furthermore, SAH is frequently complicated by hydrocephalus and vasospasm, sometimes leading to stroke.

A sentinel headache refers to a TCH that occurs days to weeks prior to a SAH. Ten to 43% of patients with aneurysmal SAH report a TCH preceding the hemorrhage.[4] However, there are substantial limitations in measuring the true incidence of sentinel headaches due to several factors: recall bias, the inability of a proportion of SAH patients to report their prior headache history, and the fact that treatment of an unruptured aneurysm prevents the SAH that is necessary for the diagnosis of a sentinel headache. Furthermore, intracranial aneurysms are present in 3 to 6% of the general population,[5] making it unclear whether aneurysms identified when evaluating TCH are symptomatic or incidental. In any case, sentinel headache has been thought to represent a “warning leak” from the weakened walls of an aneurysm. Alternatively, the pain of sentinel headache may be due to structural changes in the arterial wall that occur prior to aneurysmal rupture. If a patient presenting with TCH is found to have an unruptured aneurysm, appropriate diagnostic tests and evaluation for consideration of treatment are indicated.

Cortical SAH, in which the blood is located over the cerebral convexities rather than near the Circle of Willis, should be differentiated from aneurysmal SAH. Two small case series of cortical SAH found that none were due to aneurysms.[6,7] Cortical SAH may be associated with TCHs, reversible cerebral vasoconstriction syndrome, reversible posterior leukoencephalopathy, vasculitis, cerebral venous sinus thrombosis, abscess, and cavernoma. Because cortical SAH usually represents a secondary phenomenon due to an underlying intracranial pathology, evaluation is necessary to determine the underlying cause.[8]

CEREBRAL VENOUS SINUS THROMBOSIS

Most patients with cerebral venous sinus thrombosis (CVST) present with headache and focal neurologic symptoms due to hemorrhage and ischemia in brain regions drained by the affected veins or sinuses. Although the headache of CVST is often subacute in onset, a minority of patients present with TCH: 10 of 71 in one series presented with TCH,[9] and in another series three patients of 123 had TCH.[10] Suspicion for CVST should be greater in patients who are in the peripartum state,[11] have a known or suspected hypercoagulable disorder, or are dehydrated. Elevated opening pressure on lumbar puncture supports the diagnosis of CVST, but is not sensitive or specific.[12] Magnetic resonance venography (MRV) and the venous phase of catheter angiography are diagnostic when thrombus (or absence of blood flow) is demonstrated in a venous sinus.

CERVICAL ARTERY DISSECTION

Spontaneous carotid and vertebral artery dissections are frequently associated with headache, not infrequently TCH. Head or neck pain is present with greater than 70% of cervical artery dissections, making these the most common symptoms of cervical artery dissection.[13,14] In one-third to one-half of cases, headache precedes other symptoms, often by days or weeks.[14] Headaches are described as severe in 75% and are located ipsilateral to the dissected artery.[14] Acute-onset headaches have been identified in 22 to 60% of patients

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with cervical artery dissections.[14,15] Because dissection usually leads to ischemia in the distribution of the dissected artery, rarely do cervical artery dissections cause isolated TCH. Common neurologic symptoms and signs include lower cranial neuropathies, visual field deficits, cerebellar symptoms in vertebral dissections, amaurosis fugax, Horner syndrome, or sensorimotor deficits in carotid dissections. In suspected cases of cervical artery dissection, CT angiography (CTA), magnetic resonance (MR) angiography (MRA), catheter angiography, neck MR imaging (MRI) with fat saturation, or duplex ultrasound can be used to evaluate for true lumen narrowing or for a false lumen in the vessel wall.

STROKE

Hemorrhagic and ischemic strokes can present with TCH. Hemorrhagic strokes are more commonly associated with headache than are ischemic strokes. Two to 6% of patients presenting with TCH have intraparenchymal hemorrhage.[3,16] Headache is a feature of 19 to 27% of ischemic strokes.[17,18] Generally, headache associated with stroke is also accompanied by focal neurologic deficits, although there are isolated case reports of strokes presenting with TCH and a nonfocal neurologic exam.[19,20] In the acute setting, noncontrast CT imaging will readily diagnose intraparenchymal hemorrhage. MRI with diffusion-weighted imaging is highly sensitive for ischemic strokes.

SPONTANEOUS INTRACRANIAL HYPOTENSION

Spontaneous intracranial hypotension (SIH) is a condition of low CSF volume and/or pressure caused by CSF leaking from a dural defect, most commonly in the thoracic spine. The typical patient with SIH has a continuous diffuse headache that worsens with upright posture (sitting, standing) and improves with lying down. However, a small proportion of SIH patients present with TCH: 4 of 24 in one series,[21] 4 of 28 in another,[22] and some isolated case reports.[23,24] Symptoms commonly accompanying the headache of SIH include tinnitus, auditory muffling, neck pain and stiffness, and nausea/vomiting. A proportion of spontaneous SIH is associated with connective tissue disease, such as Marfan syndrome or Ehlers–Danlos syndrome. Thus, a family history of these diseases and physical exam indicators of connective tissue pathology (e.g., arachnodactyly, hyperextensible joints) should be sought. If lumbar puncture is performed, patients with SIH typically have a low opening pressure, although some patients may have opening pressure that still is within the population normal range. Brain MRI with gadolinium shows diffuse pachymeningeal enhancement, downward displacement of the brain (often most obvious as cerebellar tonsillar descent), crowding of the posterior fossa structures, pituitary enlargement, and engorgement of cerebral venous sinuses. Subdural fluid collections are present in as many as 50% of cases.[25] A trial of conservative treatment with supine posture, hydration, and caffeine is reasonable, although in our experience this is often insufficient. Lumbar epidural autologous blood patches are often required and may need to be repeated several times in intractable cases of SIH. Targeted blood patches or surgical repair may be indicated in patients unresponsive to lumbar epidural blood patches and in whom localization of the CSF leak has been possible.

REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME

The term *reversible cerebral vasoconstriction syndrome* was introduced in 2007 to unify and clarify an array of diagnoses all with similar clinical presentations, CSF findings, and angiographic appearance.[26] Patients with syndromes consistent with reversible cerebral vasoconstriction syndrome were previously diagnosed with different disorders based upon the specialty of the diagnosing health care provider and the setting in which the syndrome began. In the neurologic literature, patients with reversible cerebral vasoconstriction syndrome were often diagnosed with Call–Fleming syndrome. Call–Fleming syndrome,

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originally described in a small case series in 1988, was defined as severe headaches and focal neurologic deficits associated with segmental cerebral vasoconstriction, which resolved on repeat imaging.[27] It was noted that there were several disorders associated with reversible vasoconstriction without vascular infiltrate that were similar including "migrainous vasospasm," types of arteritis, postpartum headache, as well as vasoconstriction seen in association with sympathomimetics and traumatic brain injury. Over time, what had been termed benign angiopathy of the central nervous system, usually diagnosed by rheumatologists,[28,29] postpartum angiopathy, typically treated by obstetricians,[30] and reversible vasospasm without SAH[31] were also recognized to be essentially the same syndrome.

The proposed diagnostic criteria for reversible cerebral vasoconstriction syndrome have not been validated, but consist of (1) clinical presentation with thunderclap headache with or without additional neurologic symptoms or signs, (2) no evidence for aneurysmal SAH, (3) normal or near-normal (mild elevations in white blood cells and/or protein concentration) CSF, (4) angiographic (transfemoral or indirect CTA or MRA) documentation of multifocal segmental cerebral artery vasoconstriction, and (5) reversal of vasoconstriction within 12 weeks of onset.[26]

Applying these criteria, many previously separate diagnoses fall under the reversible cerebral vasoconstriction syndrome umbrella. Reversible cerebral vasoconstriction syndrome can replace various monikers for nonvasculitic narrowing of cerebral vessels, such as benign angiopathy of the central nervous system, CNS pseudovasculitis,[32] isolated benign cerebral vasculitis,[33] benign acute cerebral angiopathy,[34] migrainous vasospasm,[35,36] migraine angiitis,[37] and "crash" migraine. The use of certain drugs, particularly cannabis, sympathomimetic agents, or serotonergic agents, are often associated with the development of reversible cerebral vasoconstriction syndrome, and reversible cerebral vasoconstriction syndrome thus encompasses what was previously termed drug-induced cerebral vasculopathy, angiopathy, or arteritis.[38] Hypertension, pre/eclampsia (i.e., postpartum angiopathy), and conditions causing acute hypertension (such as pheochromocytoma) can also cause TCH due to reversible cerebral vasoconstriction syndrome.[32,39] Reversible posterior leukoencephalopathy (see below) is also seen in similar clinical situations, and can lead to similar sequelae including cortical hemorrhages and strokes.

A proportion of patients who would have been presumed to have primary TCH also have reversible cerebral vasoconstriction syndrome. One study of 56 patients with presumed primary TCH found vasoconstriction in 39%.[40] A proportion of patients with situational TCH, that is, headaches that occur only in association with a specific action or situation, have evidence for reversible cerebral vasoconstriction syndrome. Bath headache is a rare syndrome in which bathing triggers severe instantaneous headache. Reversible cerebral vasoconstriction syndrome has been demonstrated in a variable proportion of these cases, 2 of 13 in one series,[41] and ~60% in another.[42] Some of these cases also demonstrated reversible posterior leukoencephalopathy. In a case of a woman with severe hypertension and bath headache, both reversible cerebral vasoconstriction syndrome and reversible posterior leukoencephalopathy were found on imaging,[43] and in another series of four patients, one had abnormalities on MRI/MRA, consistent with reversible cerebral vasoconstriction syndrome and reversible posterior leukoencephalopathy.[44] Orgasmic TCH has been reported to be associated with reversible cerebral vasoconstriction syndrome in several cases, some of which were severe enough to produce stroke.[45–48] It is expected that with increasing availability and utilization of less-invasive angiographic techniques (MRA, CTA), as well as with increasing awareness of this diagnosis, more cases of TCH that previously would have been labeled with another diagnosis, will be correctly categorized as a reversible cerebral vasoconstriction syndrome.

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The largest case series of reversible cerebral vasoconstriction syndrome contained 67 subjects who were prospectively enrolled at a single institution over 3 years, suggesting that reversible cerebral vasoconstriction syndrome is not exceptionally rare.[49] The typical reversible cerebral vasoconstriction syndrome patient is a woman between 20 and 50 years old. However, men constituted 30% of the patients in this series, and a wide age range (19–70 years old) was seen. No cause/trigger could be identified in 37%, five cases were postpartum, and the remaining majority followed exposure to certain prescription or illicit drugs. The most common precipitants were cannabis, selective serotonin reuptake inhibitors, and nasal decongestants. This confirms previous isolated observations that serotonergic medications and pseudoephedrine may trigger cerebral vasoconstriction.[50,51] The recognized precipitants of reversible cerebral vasoconstriction syndrome are numerous (Table 2), and include common licit and illicit drugs, particularly those with serotonergic or sympathomimetic effects. Reversible cerebral vasoconstriction syndrome is not benign. Alone, or in association with reversible posterior leukoencephalopathy, reversible cerebral vasoconstriction syndrome can lead to stroke and hemorrhage.[52–55] In Ducros' series, cortical SAH was the most common complication (22%), followed by transient ischemic attack (TIA; 16%), reversible posterior leukoencephalopathy (9%), intraparenchymal hemorrhage (6%), stroke (4%), and seizures (3%). Generally, hemorrhagic events occurred early, usually in the first week; ischemic complications tended to occur later.[49] Moreover, though reversible cerebral vasoconstriction syndrome is usually limited, it can recur up to years later.[55]

The optimal treatment of reversible cerebral vasoconstriction syndrome has yet to be established. At this time, associated strokes or hemorrhages are treated as usual. Second, any precipitants are removed when possible. Third, vasospasm is treated with calcium channel blockers. Technically, the diagnosis of reversible cerebral vasoconstriction syndrome cannot be made until follow-up angiography demonstrates reversal of vasoconstriction within 3 months; however, most patients are treated presumptively once vasoconstriction is identified. Nimodipine has been used most frequently, usually orally, but sometimes intravenously (IV).[56] Recently, intraarterial nimodipine was reported in a single case to be effective in treating reversible cerebral vasoconstriction syndrome.[57] Rarely, glucocorticoids have been used,[29] particularly in instances where there may be diagnostic confusion with vasculitis, and magnesium has been used, particularly in the postpartum cases.[58] To date, there have not been trials examining the efficacy of specific treatments or the risk of secondary complications (e.g., strokes, cortical SAH) according to different treatments. Additionally, the optimal duration of treatment is unknown. A case series of 32 patients with reversible cerebral vasoconstriction syndrome utilizing transcranial Doppler showed abnormal blood velocity consistent with vasoconstriction, persisting beyond the duration of headache, suggesting that symptomatic relief with treatment does not necessarily signify reversal of vasoconstriction.[59] Further prospective studies are required to determine the optimal treatment, method of following treatment response, and the duration of treatment.

REVERSIBLE POSTERIOR LEUKOENCEPHALOPATHYY

Reversible posterior leukoencephalopathy, also termed posterior reversible encephalopathy syndrome (PRES), is due to vasogenic edema, which preferentially affects the white matter of the posterior cerebral hemispheres. Reversible posterior leukoencephalopathy occurs in association with acute hypertension, with some immunosuppressants, and has been demonstrated in pre/eclampsia. Hypertensive encephalopathy is clinically characterized by neurologic symptoms, such as confusion and visual changes in the setting of elevated blood pressure. Severe headache is present in 22% of patients with acute hypertensive crisis[60] and 53% of reversible posterior leukoencephalopathy,[61] but it is not known what proportion present with isolated TCH. Seizures and visual deficits are not uncommon, and reversible

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posterior leukoencephalopathy can lead to stroke or hemorrhage (intraparenchymal hemorrhage or cortical SAH). There is a substantial overlap between reversible posterior leukoencephalopathy and reversible cerebral vasoconstriction syndrome, in terms of triggers (hypertension, pre/eclampsia), presentation, and neurologic sequelae; in fact, a significant proportion of reported cases have both reversible posterior leukoencephalopathy and reversible cerebral vasoconstriction syndrome.[43,44,48,49]

MISCELLANEOUS CAUSES OF THUNDERCLAP HEADACHE

Increasingly, case reports of unusual etiologies of TCH are published. Retroclival hemorrhage, which is usually due to trauma, but can rarely occur spontaneously, has been identified in two case reports.[62,63] Colloid cysts of the third ventricle frequently present with TCH due to blockage of CSF flow with position change.[64] Viral or bacterial meningitis rarely presents with TCH. In a prospective study, four of 148 patients presenting with TCH were found to have an intracranial infection.[3] Most cases of intracranial infection are evident on CSF examination. Of note, however, the Erve virus was found in 10 of 72 patients presenting with TCH without SAH or CSF leukocytosis, significantly more frequently than in a control population.[65] Pituitary apoplexy presenting with TCH has been reported twice, notable because this diagnosis may be missed on CT.[66,67] Tumors usually present with focal symptoms or subacute headache, but there is a single case report of a nonhemorrhagic anaplastic oligodendroglioma associated with TCH.[68] There is one unusual case of a patient with multiple personality disorder, who had a TCH each time he switched between personalities.[69] Additional etiologies of isolated TCH reported in the literature include adult aqueductal stenosis,[70] Vogt–Koyanagi–Harada disease,[71] acute myocardial infarction,[72] sinusitis,[73] and pheochromocytoma.[74,75]

PRIMARY THUNDERCLAP HEADACHE

When the diagnostic evaluation for TCH is negative, a patient is deemed to have primary TCH. Currently, the ICHD-2 criteria for primary TCH include (1) severe head pain sudden in onset that reaches maximum intensity in less than one minute; (2) endures for one hour to 10 days; (3) does not recur regularly; and (4) is not attributed to another disorder.[1] However, a significant proportion of patients with this diagnosis have been found to have reversible cerebral vasoconstriction syndrome. Similar to reversible cerebral vasoconstriction syndrome, calcium-channel blockers may be effective in treating primary thunderclap headache. In a study of 11 cases of primary TCH, only two of whom had reversible cerebral vasoconstriction syndrome on MRA, all improved with nimodipine.[76] There is a single case report of gabapentin treating primary thunderclap headache effectively.[77] Overall, the long-term outcome of primary thunderclap headache is benign; thus, treatment is aimed at symptom relief.

DIAGNOSTIC EVALUATION OF THUNDERCLAP HEADACHE

Because the differential diagnosis of TCH is broad in scope and prognosis, the initial workup of TCH begins with a focused history and neurologic exam with special attention to features that can help prioritize the differential diagnosis. Particularly important is ascertaining the swiftness of onset of headache, rather than simply determining the severity of headache. Many patients with the “worst headache of my life” simply have a severe headache, and they do not have the suddenly maximal “thunderclap” of pain. There are no specific clinical features of a TCH or associated symptoms that reliably distinguish secondary TCH (e.g., SAH) from primary TCH.[78] Additional history of any precipitating activity, pregnancy, connective tissue disorder, hyper-coagulable disorder, medications, drugs, hypertension, and prior headaches should be sought. Examination should focus on

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eliciting focal neurologic symptoms, which when present, increase the probability of a secondary TCH.

The initial evaluation of TCH should focus on distinguishing those due to SAH. Brain CT without contrast should be undertaken without delay, as it is sensitive for ~95% cases of SAH when performed within the first 24 hours.[79] The sensitivity of CT for SAH decreases markedly with each day, as blood becomes isointense to brain parenchyma: 86% after 1 day and 76% after 2 days.[79] If CT does not show acute blood, lumbar puncture is essential to exclude a CT-negative SAH. Measurements should include opening pressure, glucose and protein concentrations, cell count, xanthochromia, and additional tests as deemed clinically necessary. As a traumatic lumbar puncture may cause the number of erythrocytes to be elevated in the CSF sample, the gradient of erythrocytes between the first and last samples should be measured. In addition, xanthochromia, as measured using wavelength spectroscopy for bilirubin, is the most reliable, with a sensitivity of 98% between 12 hours and 2 weeks after onset of TCH.[80] If spectroscopy is not available, direct visualization of the CSF for xanthochromia is performed. Estimates on the sensitivity of visual inspection for xanthochromia have varied widely.[81]

In a patient with TCH, normal exam, normal brain CT, and normal CSF, opinion is divided as to the need for further evaluation. Those who argue for watchful waiting cite the risk of stroke and other adverse events associated with catheter angiography, as well as the costs of MRI.[82] Supporting this stance are multiple follow-up studies of patients with TCH and normal exam, brain CT, and CSF, which have shown a lack of SAH and neurologic death. In a large meta-analysis of 813 such patients followed for at least one year, none had SAH or neurologic deaths.[83] In a longer study, 93 patients with “idiopathic” thunderclap headache were followed for 5 years, and none had SAH or died of neurologic causes.[84] Additionally, a study of neuron-specific enolase levels, a marker of neuronal damage, in 19 such patients found that levels were not elevated, indicating there was no neuronal injury.[85] Altogether, there are multiple data that make a case for watchful waiting in a patient with TCH and normal exam, brain CT, and CSF.

In contrast, others argue that there are several potentially disabling or dangerous conditions that present with TCH, including unruptured aneurysm, stroke, arterial dissection, CVST, reversible cerebral vasoconstriction syndrome (which can lead to stroke or hemorrhage), reversible posterior leukoencephalopathy (which can lead to stroke or hemorrhage), and others as discussed above.[86] In addition, some of these conditions are treatable, such as anticoagulation for CVST and calcium-channel blockers for reversible cerebral vasoconstriction syndrome. Furthermore, even if TCH does not indicate an ominous underlying etiology, the headache itself may recur and affect quality of life. In a large series of idiopathic thunderclap headache, half reported decreased daily functioning as a result of recurrent TCH.[84] Particularly with the increased availability of MRI and development of noninvasive angiography (MRA, CTA) and venography (MRV), one could argue that the risks of additional evaluation are minimal compared with the potential benefit of diagnosing a treatable brain disease.

Most take a middle stance, advising that clinical judgment guide the extent of workup for TCH.[87] Certainly, any unusual or worrisome aspect of the history or any potentially related abnormalities on exam call for additional workup. As noninvasive angiographic imaging techniques, such as MRA and CTA, are refined and become more readily available, it is expected that a greater proportion of TCH patients will undergo additional testing.

Additional evaluation may include MRI of the brain (including diffusion weighted imaging for stroke, gradient echo for any subacute hemorrhage, and gadolinium-enhanced images),

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together with MRA of the head and neck vessels, and MRV. This set of tests can identify most of the dangerous causes of TCH, including stroke, hemorrhage, CVST, aneurysm, dissection, reversible cerebral vasoconstriction syndrome, reversible posterior leukoencephalopathy, spontaneous intracranial hypotension, mass, pituitary apoplexy, retroclival hematoma, and sinusitis. Depending upon the institution, CTA may be more sensitive than MRA, and may be preferred, although it presents a higher risk due to radiation exposure and renal toxicity from iodine-based contrast. Conventional catheter angiography remains the gold standard. Thus, if the institutional experience has demonstrated a low risk of complications, it is reasonable to choose this modality.

CONCLUSIONS

A TCH is a severe headache of rapid onset that can indicate a serious neurologic disease or can be a benign primary headache. Initial evaluation of TCH is focused on identification of SAH. Evaluation for TCH should include brain CT followed by lumbar puncture when the CT is nondiagnostic. If CT and CSF evaluation are normal, opinion is divided as to the necessity and utility of further investigation. Further prospective studies of TCH are necessary to determine the true incidence of the various causes of TCH, the appropriate tests and procedures for a patient presenting with TCH, and the pathophysiologic processes that underlie this dramatic and alarming symptom.

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Table 1

Disorders Associated with Thunderclap Headache

Subarachnoid hemorrhage
Unruptured intracranial aneurysm
Cervical artery dissection
Ischemic stroke
Cerebral venous sinus thrombosis
Intraparenchymal hemorrhage
Spontaneous intracranial hypotension
Reversible cerebral vasoconstriction syndromes
Reversible posterior leukoencephalopathy
Infection: intracranial, sinusitis
Primary thunderclap headache

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Table 2

Recognized Precipitants of Reversible Cerebral Vasoconstriction Syndromes

Postpartum state (with or without pre/eclampsia)
Cannabis
Serotonergic drugs: ecstasy (MDMA), lysergic acid diethylamine, selective serotonin reuptake inhibitors, ergot derivatives, triptans
Sympathomimetics: cocaine, amphetamines, nasal decongestants, nicotine patches
Catecholamine-secreting tumor: pheochromocytoma, bronchial carcinoid
Binge alcohol drinking
Other medications/treatments: tacrolimus, cyclophosphamide, erythropoietin, IV Ig, interferon-α

MDMA, methylenedioxymethamphetamine; IV Ig, intravenous immunoglobulin.