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Clinical Review

THE THUNDERCLAP HEADACHE: APPROACH AND MANAGEMENT IN THE EMERGENCY DEPARTMENT

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Abstract—Background: A thunderclap headache (TCH) is a severe headache reaching at least 7 (out of 10) in intensity within 1 min of onset, and can be the presenting symptom of several conditions with potential for significant morbidity and mortality. **Objective of the Review:** This narrative review evaluates the various conditions that may present with TCH and proposes a diagnostic algorithm for patients with TCH. **Discussion:** TCH is a symptom associated with several significant diseases. The most common diagnosed condition is subarachnoid hemorrhage (SAH). Other diagnoses include reversible cerebral vasoconstriction syndrome, cerebral venous thrombosis, cervical artery dissection, posterior reversible encephalopathy syndrome, spontaneous intracranial hypotension, and several others. Patients with TCH require history and physical examination, with a focus on the neurologic system, evaluating for these conditions, including SAH. Further testing often includes head computed tomography (CT) without contrast, CT angiography of the head and neck, and lumbar puncture. Evaluation must take into account history, examination, and the presence of any red flags or signs suggestive of a specific etiology. An algorithm is provided for guidance within this review incorporating these modalities. **Management focuses on the specific diagnosis. If testing is negative for a serious**

condition and the patient improves, discharge home may be appropriate with follow-up. Conclusions: Patients presenting with TCH require diagnostic evaluation. History and examination are vital in assessing for risk factors for various conditions. Focused testing can assist with diagnosis, with management tailored to the specific diagnosis. Published by Elsevier Inc.

Keywords—headache; head CT; lumbar puncture; subarachnoid hemorrhage; thunderclap

INTRODUCTION

In the United States, headache is the fifth most common symptom presenting to the emergency department (ED) (1). While many of these headaches are benign or primary headaches, special attention is warranted for severe headaches of sudden onset, also known as a thunderclap headache (TCH). A TCH is defined as a “headache that reaches 7 (out of 10) or more in intensity within less than 1 minute” (2). TCH often occurs unexpectedly and is not preceded by any warning signs or symptoms. While the duration and location of the headache are important parts of the history, they do not have a role in defining TCH (2). Rather, the sudden intensity of the headache is the defining feature of TCH. When evaluating a patient with a headache, the emergency physician (EP) must determine both the

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intensity and time it took the headache to reach maximum severity. The EP must consider that a normal neurologic examination and absence of any associated symptoms do not exclude a serious cause in a patient with a TCH, and the patient requires a diagnostic evaluation for potentially deadly pathologic conditions (2).

METHODS

The authors searched PubMed and Google Scholar for articles using a combination of the keyword and Medical Subject Heading *thunderclap headache* for production of this narrative review, including case reports and series, retrospective and prospective studies, systematic reviews and meta-analyses, and other narrative reviews. The literature search was restricted to studies published in English. Authors decided which studies to include for the review by consensus. Initial literature search revealed more than 180 articles. A total of 84 articles were selected for inclusion in this review, focusing on ED evaluation and management of TCH. Most of the available data come from retrospective studies and case reports, with limited prospective data. As this is a narrative review, authors did not pool individual study data.

DISCUSSION

The classic teaching is that a TCH is pathognomonic for subarachnoid hemorrhage (SAH) from a ruptured intracranial aneurysm. While it is vital for the EP to consider SAH when evaluating a patient with TCH, many other dangerous conditions can present with TCH and may be missed with non-contrast head computed tomography (CT) alone (3,4). The EP must be cognizant of the different conditions that can present with TCH, as many of these conditions have significant morbidity and mortality. Importantly, a normal neurologic examination does not exclude potentially dangerous conditions in patients presenting with TCH, as close to 70% of patients with SAH will present with no neurologic deficit (5).

Differential Diagnosis

A variety of conditions can present with TCH (Table 1). This review will discuss features of these conditions, followed by an overview of the diagnosis of these specific diseases.

SAH. SAH accounts for 7–25% of patients presenting with TCH (7,8). Most cases of SAH occur from a ruptured cerebral aneurysm (about 75% of cases), which occurs most commonly at branch points in the Circle of Willis (9). The typical presentation of SAH is

a sudden, severe headache that the patient describes as the worst headache of his or her life. A headache will be the primary symptom of SAH in 70% of patients, of which 50% will present with a TCH (4,10–12). The headache usually lasts for several days and very rarely resolves within a few hours (13). Accompanying signs and symptoms include loss of consciousness (one-third of patients), seizures (6–9%), delirium (16%), stroke, visual disturbances, nausea/vomiting, dizziness, neck stiffness, or photophobia (14–16). Neck pain and stiff neck on examination are suggestive of SAH, with positive likelihood ratios (LRs) of 4.1 and 6.6, respectively (7).

A patient presenting with TCH must be evaluated for SAH due to its high morbidity and mortality. The average fatality rate of SAH is 51%, with approximately 10% of mortalities from aneurysmal SAH occurring before hospital arrival, 25% occurring within the first 24 h of SAH onset, and 45% occurring within 30 days (17,18).

A sentinel headache is a headache that occurs days or weeks prior to a ruptured cerebral aneurysm and is commonly associated with SAH (7–9). This is thought to arise from a small leak of blood into the subarachnoid space (7–9). About 10–43% of patients with aneurysmal SAH report a prior similar warning headache (19). Importantly, signs often accompanying SAH, such as a stiff neck, altered mental status, and focal neurologic deficits, are usually absent in a sentinel headache (6).

Reversible cerebral vasoconstriction syndrome. Another serious etiology of TCH is reversible cerebral vasoconstriction syndrome (RCVS). RCVS is associated with diffuse, segmental, reversible vasospasm in the central nervous system, predominantly intracranial (20,21). RCVS is thought to account for most cases of TCH that are termed *benign*, or are unexplained (2). It is a difficult diagnosis, with one study showing that patients received evaluations by up to five physicians before correct diagnosis (22). There are multiple risk factors for RCVS, including postpartum state, autoimmune diseases, sexual activity, and exposure to heat or cold. Drug exposures related to RCVS include immunosuppressive drugs, ergotamine, triptans, selective serotonin reuptake inhibitors, pseudoephedrine, cocaine, amphetamines, ecstasy, cannabis, and bromocriptine (23–31).

The hallmark of RCVS is multiple TCHs that recur every day or every few days. These headache recurrences can occur for up to 4 weeks (20,31). While RCVS can present identically to SAH, the duration of headache is usually shorter than SAH, typically lasting several hours (20,32). This feature, along with identification of RCVS triggers and history of sudden-onset headaches over the past days to weeks can help differentiate RCVS from SAH. Other symptoms include altered mental status, motor or sensory deficits, seizures, visual

Table 1. Features and Diagnosis of Conditions Associated With Thunderclap Headache (1,2,5,6)

Condition	Features	Diagnostic Testing
Subarachnoid hemorrhage	Sudden onset/maximal headache Neck pain by history or neck stiffness on examination	Head CT (within 6 h)* LP if headache onset > 6 h prior to presentation or in high clinical suspicion
Reversible cerebral vasoconstriction syndrome	Transient loss of consciousness Multiple presentations with TCH, which last hours and recur over weeks Risk factors for RCVS: postpartum state, autoimmune diseases, sexual activity, exposure to extreme heat/cold, specific medications TCH only lasts several hours	Head CTA or MRA
Cerebral venous thrombosis	Hypercoagulable state, including postpartum or recent surgery Papilledema, altered mental status, seizures, neurologic deficit Patients often younger than 50 y Lumbar puncture with elevated opening pressure	CT or MR venogram
Cervical artery dissection	Neck pain in addition to headache History of recent neck trauma or manipulation History of connective tissue disease, large-vessel arteriopathies, hypertension, migraines	Head and neck CTA
Posterior reversible encephalopathy	Headache, seizures, visual loss, extreme hypertension	Brain MRI
Spontaneous intracranial hypotension	Recent spinal procedure Positional headache (improved in supine position)	Brain MRI (with and without contrast)
Pituitary apoplexy	History of pituitary adenoma Ophthalmoplegia, vomiting, decreased visual fields	CT (within first 2 h of headache onset for acute hemorrhage); if negative, MRI
Third ventricle colloid cyst	TCH that rapidly resolves Signs of hydrocephalus or elevated intracranial pressure	Brain MRI

CT = computed tomography; CTA = computed tomography angiography; LP = lumbar puncture; MR = magnetic resonance; MRA = magnetic resonance angiogram; MRI = magnetic resonance imaging; RCVS = reversible cerebral vasoconstriction syndrome; TCH = thunderclap headache.

* Other causes include temporal arteritis; acute angle closure glaucoma; retroclival hematoma; meningitis; complicated sinusitis; cluster headache; and primary cough, exertional, and sexual headaches.

changes, ataxia, speech abnormalities, and nausea or vomiting (6).

While the headache from RCVS is usually self-limiting, it is not always benign. A minority of patients can experience residual effects, including seizures or strokes (20,32,33).

Cerebral venous thrombosis. While the onset of headache in cerebral venous thrombosis (CVT) is usually gradual, 2–13% of patients experience a TCH as the primary symptom (34). Signs and symptoms of CVT include seizures (more commonly focal), papilledema, altered mental status, and focal neurologic deficits (6). The symptoms can be associated with thrombus location (35,36). Importantly, patients with CVT presenting with TCH as their main symptom may be clinically indistinguishable from patients with SAH presenting with TCH, reinforcing the importance of maintaining a broad differential in a patient with TCH (6).

While CVT is a relatively rare disorder, 80% of patients with CVT are younger than 50 years old (35,37,38). The mean age of diagnosis is 39 years (39). CVT is more common in women, especially in the peri-

partum period and in patients with recent surgery (40). CVT is also associated with hypercoagulable states, including the use of oral contraceptives, hematologic disorders, factor V Leiden, protein C or S deficiency, and anti-thrombin III deficiency; however, a significant number of patients will not possess a risk factor (35–40).

Cervical artery dissection. A cervical artery dissection encompasses carotid or vertebral artery dissection. While headache onset is typically gradual in a patient with a cervical artery dissection, TCH occurs in 5–20% of patients (41–43). A cervical artery dissection can result in an ischemic stroke, transient ischemic attack, or more rarely an SAH (6). Carotid or vertebral artery dissections are an especially important cause of stroke to consider in young and middle-aged patients (44–48). A significant risk factor is a history of neck trauma, which can be minor (e.g., manipulation therapy of the neck or sports-related trauma) (47,48). Other risk factors include connective tissue disease, large-vessel arteriopathies, hypertension, and a history of migraines (48–51).

According to the International Headache Society's diagnostic criteria, headaches from cervical artery

dissection must be ipsilateral to the dissected artery (52). The typical first symptom of a cervical artery dissection is unilateral headache (68%), neck pain (39%), or facial pain (10%) (53). Additionally, approximately 25% of patients will experience a partial Horner's syndrome (miosis and ptosis) (54). A vertebral artery dissection presents with neck pain (66%) and headache (65%), which can be unilateral or bilateral (55). The headache is more commonly posterior in location. Many other symptoms may be present, including facial paresthesia, dizziness, vertigo, nausea/vomiting, visual disturbances (such as diplopia), ataxia, limb weakness or numbness, dysarthria, and hearing loss (41,43,53).

Posterior reversible encephalopathy syndrome. Several case reports describe patients who presented with TCH from either a hypertensive crisis or posterior reversible encephalopathy syndrome (PRES) (56,57). PRES is a clinical syndrome with radiographic findings that presents with headache, seizures, and visual loss, often with extreme hypertension (58). The headache associated with PRES generally has an acute onset (8). Specific radiographic findings are necessary for the diagnosis, and include symmetric edema of the white matter in the posterior cerebral hemispheres (59).

Spontaneous intracranial hypotension. Fifteen percent of patients with spontaneous intracranial hypotension will present with TCH (60,61). The most common cause of spontaneous intracranial hypotension is cerebrospinal fluid (CSF) leakage from spinal meningeal defects or dural tears (61). This most commonly occurs after lumbar puncture (LP), but can occur from minor trauma such as falls, lifting, coughing, or sports (2–6). Most commonly, intracranial hypotension presents with a positional headache that improves after lying down and worsens when upright (62).

Pituitary apoplexy. Pituitary apoplexy occurs with hemorrhage or infarction of the pituitary gland (2,6). This most commonly occurs in the setting of a pituitary adenoma, but may occur in association with pregnancy, head trauma, dopamine agonist therapy, or pituitary radiation (63). Pituitary apoplexy usually presents with a combination of acute headache, vomiting, ophthalmoplegia, decreased visual acuity, reduction in visual fields, and altered mental status (64). The headache is usually sudden and severe (64).

Third ventricle colloid cyst. A colloid cyst of the third ventricle can impede the flow of CSF leading to obstructive hydrocephalus. Third ventricle colloid cysts account for 0.5% of intracranial tumors and are most commonly diagnosed between the third and fifth decades of life

(65). The most common symptom is headache, which occurs in 68–100% of patients (66). The headache of a third ventricle colloid cyst usually begins abruptly, lasts for seconds up to 1 day, and resolves quickly (67). The headache may be relieved with a supine position. Additionally, 50% of patients have associated nausea/vomiting. Patients may also experience loss of consciousness, altered mental status, seizures, coma, or death (66).

Other causes of TCH. Multiple other conditions have been reported to present (rarely) as TCH. These conditions include temporal arteritis; acute angle closure glaucoma; retroclival hematoma; meningitis; complicated sinusitis; cluster headache; and primary cough, exertional, and sexual headaches (2,5).

Diagnostic Evaluation

Due to the large number of conditions that can present with TCH, identifying the definitive etiology can be difficult, and there is no accepted algorithm for the evaluation of a patient presenting with TCH. Even with a thorough evaluation, studies suggest that a diagnosis is made in only 27–71% of patients with TCH (3,5,6,10). The most commonly diagnosed cause of TCH is SAH (3,5,6,10). Other vascular causes are the second most commonly diagnosed, which include cervical artery dissection, CVT, and RCVS (2,68).

Figure 1 presents a proposed diagnostic algorithm for patients presenting with TCH. As many patients present to the ED with a headache, the initial step is correctly identifying the headache as a TCH (did the headache reach 7 out of 10 pain or greater within 1 min?). Patients presenting with TCH should be evaluated for SAH due to the high morbidity and mortality of the condition. If the EP is concerned for cervical artery dissection or RCVS (e.g., multiple episodes of TCH, neck pain, or Horner's syndrome), initial imaging should begin with a noncontrast head CT in addition to a CT angiography (CTA) of the head and neck. CTA head and neck is the diagnostic modality of choice for cervical artery dissection. While helpful for RCVS, the EP must keep in mind that initial imaging may be negative, especially if the patient is presenting within the first week of headache onset (20).

In addition to a noncontrast head CT, CTA head and neck may aid in the diagnosis in SAH. In a small study, 2 of 116 patients were diagnosed with an aneurysm thought to be causing SAH after both normal imaging by head CT and negative LP (69). The probability of excluding an SAH following negative CT/CTA is 99.4% (70). The disadvantage of obtaining a CT/CTA is that 2–5% of individuals have an incidental aneurysm, the significance of which is unclear (71,72). A patient whose imaging reveals an aneurysm may still require

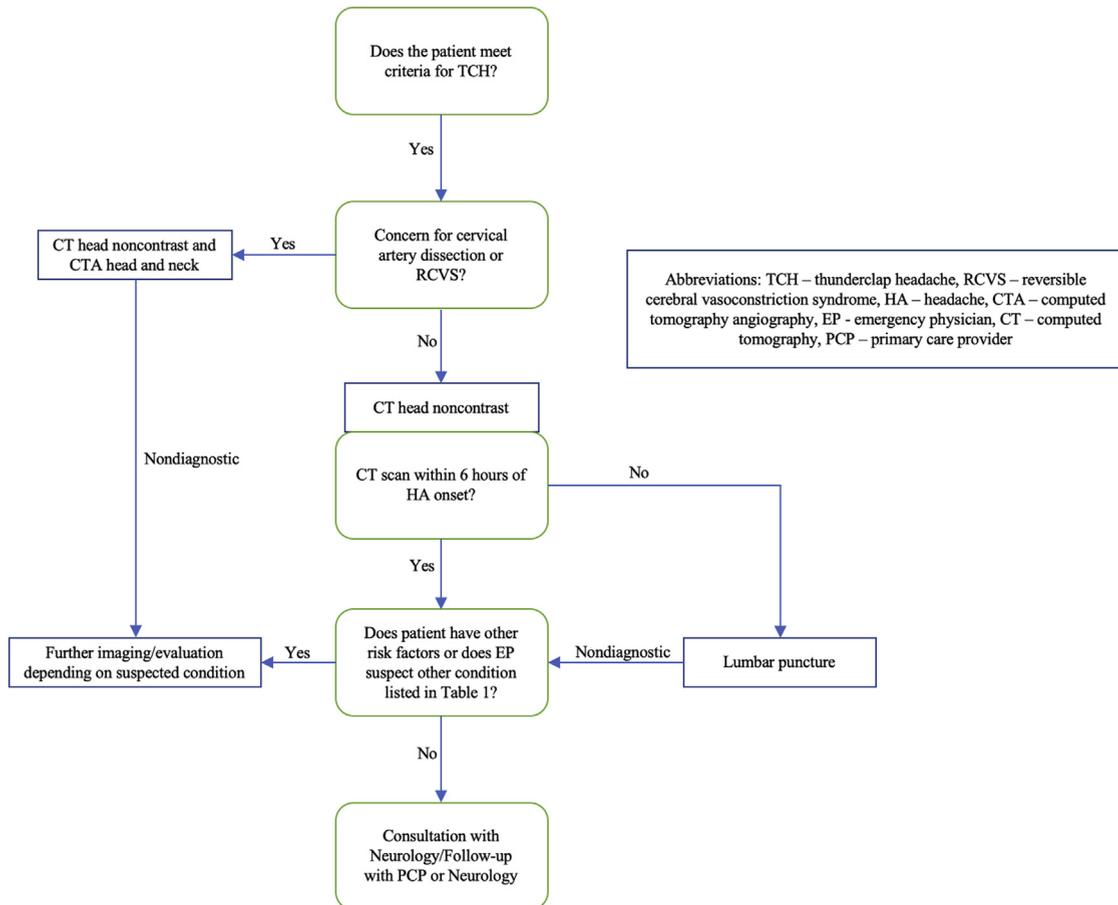


Figure 1. Diagnostic evaluation of thunderclap headache.

LP to evaluate for SAH. While it may be unclear whether the aneurysm is responsible for the headache, a systemic review demonstrated that symptomatic aneurysms had a relative risk of rupture of 8.3 compared to asymptomatic aneurysms (72). A patient with an aneurysm on imaging should be referred to a neurosurgeon.

If the EP has low concern for cervical artery dissection or RCVS, the patient should receive a noncontrast head CT for initial evaluation. CT has a high sensitivity and specificity for SAH, a time-sensitive diagnosis. When conducted within 6 h of onset of TCH, CT has a specificity of 98% and sensitivity nearing 100% for diagnosis of SAH (11). A CT conducted within 6 h of headache onset and read by an attending radiologist as negative has a LR⁻ of 0.01, essentially ruling out SAH (7,73). As time from headache onset increases, the sensitivity of head CT for SAH declines, with a sensitivity of 86% on day 2, 76% after 2 days, and 58% after 5 days (74). There are several other factors to consider when omitting the LP in patients with negative head CT within 6 h of headache onset. The patient should have a normal neurologic examination, as focal neurologic deficits are associated with both SAH and other intracranial

pathologic conditions. Additionally, the patient's hematocrit must be $\geq 30\%$, as patients with hematocrit $< 30\%$ may have blood that appears isodense on head CT (73). The CT scanner should be third generation or newer, the physician interpreting the scan should be an attending-level radiologist, and the EP must communicate the clinical concern of SAH to the radiologist interpreting the study (73–75). If the EP is considering omitting the LP in a patient with a negative head CT presenting within 6 h of headache onset, the risks and benefits of this diagnostic strategy must be communicated to the patient. Importantly, the patient must be informed of the remaining risk for SAH of approximately 1 per 1000 (7,70).

LP

An LP with opening pressure can aid in determining the etiology of the TCH. LP is the gold standard for the diagnosis of SAH, especially if the patient is evaluated 6 h or more after headache onset (11,75). LP after nondiagnostic head CT is recommended by the American College of Emergency Physicians Clinical

Policy for evaluation of SAH (76). The LP should include opening pressure, CSF studies, and an analysis for xanthochromia. Classic LP findings in SAH include an elevated opening pressure, elevated red blood cell (RBC) count that does not decrease from tube 1 to tube 4, and xanthochromia. Unfortunately, traumatic LP occurs in approximately 15% of cases, which can muddle the diagnosis (77). Additionally, there is no absolute threshold for RBC cutoff or clearing from tube 1 to tube 4 for diagnosing SAH. One study found no patients with SAH with RBC count $< 100 \times 10^6/L$ in tube 4 (78). This study also found a 63% reduction in RBCs from tube 1 to tube 4 to be the optimal threshold for clearance, but this has not been externally validated (60,78,79). Additionally, the CSF should be visually inspected for xanthochromia. Xanthochromia is formed by the breakdown of hemoglobin and can take 2–12 h to develop. Up to 20% of patients with SAH who receive an LP within 6 h of headache onset will have positive xanthochromia, which approaches 100% after 12 h from headache onset (80,81). One study found that the combination of no xanthochromia and CSF RBC count $< 2000 \times 10^6/L$ had an LR⁻ of 0 (82). In addition to no clear diagnostic criteria of LP for SAH, LP is invasive and has complications (70,83). The procedure is complicated by post-LP headache in up to 32% of patients (83). Additionally, the procedure can be time consuming and difficult to perform in obese or uncooperative patients.

LP can aid with diagnoses other than SAH. Opening pressure can help narrow the differential diagnosis, as CVT may be associated with an elevated opening pressure, while intracranial hypotension is associated with a low opening pressure (2,36). CSF studies, including glucose, protein, RBCs, white blood cells, differential, cultures, and meningitis/encephalitis panels, can be used for diagnosing SAH and meningitis. However, in other disease processes, such as RCVS and pituitary apoplexy, LP is typically not helpful.

Alternate Diagnosis Strategies

Noncontrast CT can miss many causes of TCH, including SAH (especially if the patient presents more than 6 h after headache onset), CVT, cervical artery dissection, PRES, intracranial hypotension, pituitary apoplexy, and a third ventricle colloid cyst. For CVT, the initial CT may be normal in up to 25–30% of patients (84). In a patient with cervical artery dissection without an ischemic stroke, head CT is usually normal (2,6). The ideal imaging modality for each condition presenting with TCH is shown in Table 1.

If the CT, and potentially the LP, is nondiagnostic, the EP must consider alternative diagnoses. The EP should

engage in shared decision making with the patient for potential evaluation of alternative diagnoses. If the patient's history or examination has features concerning for another diagnosis, or if the EP suspects another diagnosis (Figure 1), an alternate imaging strategy should be pursued depending on the concern (Table 1). Further diagnostic evaluation may be made in conjunction with a neurologist. Regardless of whether an alternate imaging strategy is pursued, the patient should be referred to a neurologist for additional evaluation, especially if the patient has experienced multiple episodes of TCH.

CONCLUSIONS

A TCH is a headache that reaches 7 (out of 10) or more in intensity in < 1 min. Patients presenting with TCH must be evaluated for a life-threatening intracranial condition. As many conditions can present with TCH (most commonly SAH or RCVS), a thorough history is essential in evaluating for risk factors for other conditions. The EP must consider that the absence of associated symptoms and a normal physical and neurologic examination do not exclude a serious cause in a patient with a TCH; the patient still requires diagnostic evaluation. Due to the high morbidity and mortality of SAH, patients presenting with TCH must be evaluated for SAH. If concerned for cervical artery dissection or RCVS, diagnostic evaluation should begin with a CT/CTA. Otherwise, a noncontrast head CT should be the initial imaging modality. A noncontrast head CT has a sensitivity for SAH nearing 100% if performed within 6 h of headache onset. Depending on the timing of the headache and other factors, evaluation may also include LP. The patient history and presentation should guide further diagnostic evaluation. Additionally, decisions on additional imaging and diagnostic evaluation should be made with shared decision making with the patient and in conjunction with a neurologist.

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ARTICLE SUMMARY

1. Why is this topic important?

Thunderclap headache (TCH) is a severe headache that can be the presenting symptom of several conditions with potential for severe morbidity and mortality.

2. What does this review attempt to show?

This narrative review evaluates several conditions associated with TCH and provides recommendations for emergency department (ED) investigation of the patient with TCH.

3. What are the key findings?

TCH is a severe headache reaching at least 7 (out of 10) in intensity within 1 min of onset, associated with subarachnoid hemorrhage, reversible cerebral vasoconstriction syndrome, cerebral venous thrombosis, cervical artery dissection, posterior reversible encephalopathy, spontaneous intracranial hypotension, and several others. Focused history and physical examination supplemented with diagnostic assessments including imaging are necessary. Further testing often includes head computed tomography (CT) without contrast, CT angiography of the head and neck, and lumbar puncture. Specific testing and management are based on the clinical situation and suspected diagnosis.

4. How is patient care impacted?

This review investigates several potentially deadly diseases associated with TCH and provides recommendations for ED evaluation of patients with TCH. Focused testing can assist with diagnosis, with management tailored to the specific diagnosis.