The Patient with Thunderclap Headache

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**KEYWORDS**
- Thunderclap headache
- Subarachnoid hemorrhage
- Lumbar puncture
- Intracranial aneurysm

**KEY POINTS**
- Thunderclap headache (sudden onset of severe headache reaching maximal intensity within seconds to a minute) can have multiple causes, but aneurysmal rupture causing subarachnoid hemorrhage is the primary concern.
- Noncontrast CT performed within 6 hours of onset is very sensitive for subarachnoid hemorrhage, but the sensitivity decreases with time.
- Further work-up for subarachnoid hemorrhage should be guided by the pattern of blood on noncontrast CT head.

Headache is an extremely common symptom and annually more than 70% of the United States population may have a headache.\textsuperscript{1} Headache accounts for approximately 2% of all emergency department (ED) visits.\textsuperscript{2} Most episodes of headache are benign and do not require emergent imaging.\textsuperscript{3} Clinical decision rules have been proposed to identify patients with acute nontraumatic headache who need further investigation.\textsuperscript{4} Despite high sensitivity for subarachnoid hemorrhage (SAH), they suffer from poor specificity and are applicable to only a minority of ED patients with headache.\textsuperscript{5} In a 2006 study, 14% of patients presenting with headache underwent neuroimaging, and only 5.5% of the imaged patients received a pathologic diagnosis.\textsuperscript{2}

Thunderclap headache (TCH) is defined as sudden-onset unruptured intracranial aneurysm (UIA) of severe headache reaching maximal intensity within seconds to a minute.\textsuperscript{6} The term TCH was initially used in reference to pain associated with a UIA, but multiple causes have since been described (Boxes 1 and 2, Table 1).\textsuperscript{6,7} Aneurysmal rupture resulting in SAH is the primary concern, given the high morbidity and mortality associated with this condition.\textsuperscript{8} It accounts, however, for only 4% to 12% of acute, severe headaches.\textsuperscript{9–12} Primary TCH is a diagnosis of exclusion when all other underlying causes have been eliminated. Primary TCH can recur intermittently but is generally associated with a benign outcome.\textsuperscript{6} This review discusses the differential diagnosis of TCH and details the...
diagnostic assessment of patients presenting with TCH.

**DETECTION OF SUBARACHNOID HEMORRHAGE**

SAH results most commonly from rupture of an intracranial aneurysm. Headache associated with SAH typically lasts a few days; it is atypical for the headache to resolve in less than 2 hours. Loss of consciousness can occur in a third of patients with SAH. Other symptoms may include nausea, vomiting, dizziness, photophobia, neck stiffness, delirium, and seizures. Prompt diagnosis of acute SAH is critical because initial misdiagnosis and subsequent rebleeding correspond with a poor prognosis and up to 70% mortality. SAH may go undiagnosed in 5% of patients during ED visits, with lower acuity patients at higher risk.

**Table 1**

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<td>Possibly presenting with normal CT results and normal or near-normal results of analysis of CSF</td>
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suspected SAH. The sensitivity of CT for detecting acute SAH is 90% to 100% when performed within 24 hours but decreases with time as blood is progressively diluted by normal cerebrospinal fluid (CSF) flow. In patients presenting with TCH and normal neurologic examination, a normal brain CT within 6 hours of headache onset is extremely specific in ruling out aneurysmal SAH. Beyond 6 hours, the reported sensitivity of CT is 89%. Patients with atypical features (syncope and seizures), focal neurologic deficits, or CT performed beyond 6 hours of onset do need further work-up after a negative noncontrast CT Head.

Negative CT in patients with SAH is often attributed to delayed clinical presentation, very small volumes of initial hemorrhage, or a low hematocrit. Certain locations, such as the interpeduncular cistern, and small, focal convexity bleeds are more likely overlooked. Posterior temporal horn dilatation has been reported as a prevalent finding in 66% to 84% of SAH cases, even in the absence of visible hemorrhage. Mark and colleagues reported that in a recent survey favored undergoing a CTA instead of LP after a nondiagnostic noncontrast CT. The utility and cost-effectiveness of CTA to replace LP in this situation, however, have been questioned. A recent meta-analysis reported the pooled sensitivity and specificity for CTA to detect aneurysms of 98% and 100%, respectively; 75% of patients in a recent survey favored undergoing a CTA instead of LP after a nondiagnostic noncontrast CT. CTA is associated with radiation risks and requires administration of iodine-based contrast, which can be nephrotoxic. There is an approximately 3.2% prevalence of unruptured aneurysms in the general, non–high-risk population. More recent studies with liberal use of magnetic resonance angiography (MRA) report a prevalence as high as 7% in large, population-based studies. A significant proportion (up to 87.6%) of incidental UIAs have been reported to be small, measuring less than 3 mm to 4 mm. Small aneurysms (<7 mm) uncommonly cause symptoms and are most frequently incidentally detected. No studies have sufficiently correlated presentation with headache with change in risk of spontaneous hemorrhage in unruptured aneurysms, and most headaches in UIAs are not directly related to the aneurysm. Treatment or imaging surveillance of these incidentally detected UIAs is not without significant costs and complications. Although CTA is frequently performed in clinical practice, current guidelines still recommend LP as the next diagnostic test after initial negative head CT.

MR imaging can be sensitive for the detection of SAH; T2 fluid-attenuated inversion recovery (FLAIR) is sensitive in the acute phase, and subarachnoid blood products display sulcal hyperintensity. It may fail, however, to demonstrate blood in tight cisterns, and there are
multiple causes of sulcal hyperintensity on FLAIR other than hemorrhage.\textsuperscript{45,46} T2* sequence has been demonstrated as having a sensitivity of 94\% within 4 days of ictus, but a 100\% sensitivity between 4 days and 14 days, with a high specificity.\textsuperscript{47} MR imaging is not recognized, however, as sufficiently sensitive to discard LP.\textsuperscript{48}

**FURTHER WORK-UP OF SUBARACHNOID HEMORRHAGE**

Multidetector CTA is an accurate and sufficient tool for detecting and characterizing aneurysms in the setting of acute SAH.\textsuperscript{49,50} CTA has largely replaced digital subtraction angiography (DSA) for detection of intracranial aneurysms in most patients.\textsuperscript{51} The reported sensitivity, specificity, and accuracy of aneurysm detection with modern-generation scanners have improved dramatically.\textsuperscript{52} When CTA is negative, DSA is still performed at many institutions due to concern that an intradural aneurysms may be missed.

**ANEURYSMAL SUBARACHNOID HEMORRHAGE**

Ruptured aneurysms account for 85\% of SAH cases; 10\% to 43\% of patients with aneurysmal SAH have a history of a sentinel headache or warning leak days to weeks before detection of aneurysm rupture.\textsuperscript{53} The most common locations for aneurysm are anterior communicating artery, middle cerebral artery bifurcation, posterior communicating artery, and the terminal basilar artery.\textsuperscript{55} High volume of hemorrhage localized to the basilar cisterns is indicative of aneurysmal SAH, and patterns of hemorrhage help predict site of aneurysm\textsuperscript{56} (Fig. 1). Although SAH usually occurs at the same location as cerebral aneurysm, location of SAH is not always a reliable indicator of site of aneurysm rupture, with the exception of...
angiographic imaging is essential. In patients with perimesencephalic bleeding pattern, initial prior circulation aneurysms can present with a false-negative result, or missed diagnosis due to error. Aneurysms that may potentially be missed on initial CTA include those at the skull base, small bifurcation aneurysms, those on a curve of a vessel, perforator aneurysms, and small, infectious, or myxomatous aneurysms. The sensitivity of CTA for detection of aneurysms depends on the arterial attenuation of vessels. Repeat DSA is recommended in patients with diffuse, nonperimesencephalic pattern of SAH, although the timing of repeat angiography is subject to debate. Even in patients with negative initial 3-D rotational angiography for aneurysmal type SAH, repeat 3-D rotational angiography may show a ruptured aneurysm in 1 in 4 patients.

Cranial MR imaging performed within 72 hours, or on a delayed basis, for an angiogram-negative SAH has a low diagnostic yield and is not routinely recommended. High-resolution vessel wall–MR imaging has so far not been shown to alter management in angiogram-negative SAH patients, although it is increasingly used to identify the ruptured lesion when a CTA reveals multiple aneurysms.

PERIMESENCEPHALIC HEMORRHAGE

Two-thirds of the nonaneurysmal SAH patients may have perimesencephalic hemorrhage with blood confined to the perimesencephalic cisterns. Perimesencephalic hemorrhage is blood confined to the interpeduncular, preopticine, ambient, quadrigeminal, or premedullary cisterns, with possible extension to the proximal stems of the sylvian fissure but no deep extension into the anterior interhemispheric fissure or lateral aspect of sylvian fissures. Perimesencephalic hemorrhage patients usually have a better clinical grade at presentation, no neurologic deficits, and generally a good prognosis. Because approximately 10% of posterior circulation aneurysms can present with a perimesencephalic bleeding pattern, initial angiographic imaging is essential. In patients meeting the strict imaging criteria of perimesencephalic hemorrhage, however, initial negative CTA has been shown reliable and cost-effective in excluding aneurysms, without need for further angiographic work-up. Recurrence is extremely rare and does not reveal aneurysms on further imaging, and patients have a good prognosis compared with aneurysmal SAH. American Heart Association/American Stroke Association guidelines suggest that DSA may not be necessary if a classic perimesencephalic pattern of hemorrhage is present and CTA may suffice.

PERIPHERAL, CONVEXITY SUBARACHNOID HEMORRHAGE

Subarachnoid blood restricted to 1 or more cerebral sulci without extension to the basal cisterns, ventricles, or sylvian and interhemispheric fissures represents a distinct group of patients with nontraumatic SAH. Reversible cerebral vasoconstriction syndrome (RCVS) is increasingly recognized as the most common cause of convexity SAH in patients 60 years or younger, with amyloid angiopathy the leading cause in older patients. Amyloid angiopathy patients typically do not present with recurrent headaches. Cerebral venous thrombosis (CVT) and arterial dissection can also present with TCH and small, convexity bleeds and do not show up on CT or CSF analysis. MR imaging and craniocervical angiography may be needed in these cases. Mycotic and oncotic aneurysms in the distal vasculature can also present as convexity, sulcal SAH. Cross-sectional imaging has a poor sensitivity in detection of abnormalities in distal vasculature, including aneurysms, dissections, and dural arteriovenous fistulae, and conventional angiography is frequently needed.

REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME

RCVS is characterized by severe headaches, with or without acute neurologic symptoms, and diffuse segmental constriction of cerebral arteries that resolves spontaneously within 3 months. More than half of cases occur postpartum or after exposure to adrenergic or serotoninergic drugs. Many patients have a history of migraine, and acute migraine treatments (triptans and ergots) can precipitate RCVS or aggravate the vasoconstriction when the TCH is mistaken for a migraine attack. Severe headaches typically are short lived (usually lasting 1–3 hours) and recur for 1 week to 2 weeks, with a self-limiting course, and no new symptoms typically occur after 1 month. Triggering event for the headache maybe...
sexual activity, straining during defecation, stressful or emotional situations, coughing, sneezing, showering, and sudden bending down. The course is uniphasic, but the manifestations can vary from pure cephalgia to rare catastrophic forms complicated by ischemic and hemorrhagic strokes. The clinical-radiologic features tend to be dynamic with

Fig. 2. Perimesencephalic hemorrhage. Axial CT (A, B) demonstrating hyperdense blood in the interpeduncular, ambient, and preponine cisterns. CTA (C) and DSA (D) did not reveal any vascular etiology for the perimesencephalic blood.
cerebral vasoconstriction at its peak on angiograms obtained 2 weeks to 3 weeks after clinical onset.71

Brain scans of many patients with RCVS do not show focal abnormalities despite presence of diffuse vasoconstriction on angiography, especially on initial imaging.77 The spectrum of imaging findings described are reversible edema, convexity SAH, intracerebral hemorrhage, and cerebral infarction.71 Parenchymal hemorrhages are more frequently single than multiple and lobar than deep. They occur early in the course of RCVS and are associated with focal deficits.78 Cerebral infarctions typically occur in arterial watershed regions and occur later than hemorrhagic strokes in the course of RCVS.75 Edema is an early manifestation of RCVS, with distribution similar to that of posterior reversible encephalopathy syndrome and usually totally reverses within 1 month of onset, earlier than does vasoconstriction.71 Reversible brain edema occurs in 8% to 38% of all cases of RCVS, whereas multifocal cerebral vasoconstriction has been noted in more than 85% of patients with posterior reversible encephalopathy syndrome.79

The arteriopathy is typically bilateral and diffuse and frequently disproportionate and distant to the small, focal amount of subarachnoid blood.80 The imaging findings of SAH along with cerebral vasoconstriction can be easily confused with other entities, such as vasospasm after aneurysmal SAH and vasculitis. The clinical features, CSF characteristics, and distinctive pattern of imaging on DSA, however, can generally easily help with characterization. Arterial changes in RCVS are typically widespread, involving smaller/distal vessels, and disproportionately excessive compared with small amount of SAH seen on the CT or MR imaging. In contrast, vasospasm is typically observed in patients with higher Fisher scale grade SAH patients, predominates in the large vessels of circle of Willis, and generally peaks between days 4 and 12 after SAH. In RCVS patients, initial angiographic study maybe normal if performed early, even in presence of brain edema or hemorrhage. Maximum vasoconstriction has been reported in branches of middle cerebral arteries after 2 weeks of clinical onset81 (Fig. 3). The arterial narrowing is not fixed, with new constrictions seen on subsequent angiography often affecting more proximal vessels.71 High-resolution MR imaging vessel wall imaging may help distinguish RCVS (uniform wall thickening with negligible to mild enhancement) from central nervous system (CNS) vasculitis (concentric or eccentric wall enhancement).82

Fig. 3. RCVS. MR imaging FLAIR images (A, B) demonstrating sulcal hyperintensity due to SAH and corticocentral subcortical edema in posterior distribution. Time-of-flight MRA (C) showing areas of irregularity and narrowing most prominent in left M2 (arrow). DSA performed at 3 weeks (D–G) showing beading with more prominent areas of stenosis and beading involving more proximal circle of Willis.
PRIMARY ANGIITIS OF THE CENTRAL NERVOUS SYSTEM

Primary CNS angiitis usually has an insidious onset in contrast to RCVS. Headaches are not typically thunderclap and are followed by stepwise deterioration with focal deficits, infarcts, or cognitive decline. TCH rarely is seen with a ruptured aneurysm associated with vasculitis. Abnormal results of CSF analysis are seen in 80% of patients with primary angiitis, whereas they are normal or near normal in patients with RCVS. MR imaging is abnormal in most cases and shows several small deep or superficial infarcts of different ages, with or without white matter abnormalities and/or parenchymal enhancing lesion. High-resolution black-blood MRA may depict concentric or eccentric areas of vessel wall enhancement. Arterial irregularities typically involve the third-order or fourth-order branches of the circle of Willis. These irregular areas of narrowing are not as dynamic and do not change or improve as rapidly as in RCVS.

CEREBRAL VENOUS THROMBOSIS

Although headaches are a common presentation in patients with CVT, only 2% to 10% have TCH as predominant symptom. Headaches are frequently persistent and exacerbated by...
increased intracranial pressure (caused by coughing, sneezing, or Valsalva maneuver) or in recumbent position; 10% of patients with CVT can present with SAH, usually focal and localized to few convexity sulci. It is uncommon, however, to see SAH as a sole imaging finding in CVT. CT abnormalities can be seen in 90% of patients with focal neurologic deficits and include venous infarcts, edema, or hyperdensity within the occluded sinus (Fig. 4). Hemorrhage in venous thrombosis is typically cortical with subcortical extension. MR imaging with venography is commonly needed for diagnosis of CVT and should be considered when clinically concerned for venous thrombosis. CT venography is a reasonable alternative. DSA is generally not necessary for diagnosis but is generally used in treatment of refractory patients that are considered for endovenous thrombolysis.

CERVICAL ARTERY DISSECTION

Headache is reported in 60% to 95% of patients with arterial dissections and up to 20% present with TCHs. Neck pain is frequently associated. Associated findings include amaurosis fugax, Horner syndrome, pulsatile tinnitus, dysgeusia,
diplopia, and other stroke manifestations.\textsuperscript{6} Dissections resulting in SAH are more common in the posterior circulation and in children.\textsuperscript{87} Brain CT and LP are usually normal and ultrasound, CTA, or MRA should be considered when clinically concerned for dissection. Angiographic features include luminal narrowing, vessel irregularity, wall thickening/mural hematoma, intimal flap, and pseudoaneurysm formation (Fig. 5). Up to 7\% of patients with arterial dissections can present with self-limiting, convexity SAH.\textsuperscript{88}

**SPONTANEOUS INTRACRANIAL HYPOTENSION**

Spontaneous intracranial hypotension usually presents as orthostatic headaches, which worsen when upright and improves after lying down. However, 15\% of spontaneous intracranial hypotension patients can present with TCH.\textsuperscript{71} Brain MR imaging reveals diffuse pachymeningeal thickening and enhancement, in addition to brain sagging and cerebellar tonsillar descent (Fig. 6). Crowding of the posterior fossa, reduction in prepontine space, descent of optic chiasm, and subdural collections may also be present.\textsuperscript{89}

**ARTERIOVENOUS MALFORMATION**

Less than 5\% of ruptured arteriovenous malformations (AVMs) can present as SAH without intracerebral hematoma.\textsuperscript{13} SAH as a presentation is more likely when aneurysms occur in

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**Fig. 6.** Sagittal T1WI (A) shows brain sagging with effacement of suprasellar and prepontine cisterns, cerebellar tonsillar ectopia, and sharp angulation at the junction of internal cerebral veins with straight sinus. Bilateral subdural collections seen on FLAIR (B) and axial T2 (C) with effacement of basal cisterns and deformation of brainstem. Sagittal postcontrast image (D) shows pituitary engorgement and prominent venous sinuses. Diffuse pachymeningeal enhancement on axial postcontrast image (E).
association with AVM. These aneurysms can be characterized as (1) proximal or distal, flow related, (2) intranidal, or (3) unrelated. Flow-related aneurysms occur more frequently, but intranidal aneurysms present with bleeding more often. Serpiginous hyperdense structures representing dilated vasculature in the periphery of brain parenchyma, with or without associated calcifications, on unenhanced CT should raise concern for an AVM. This can be easily confirmed with CTA or MR imaging of the brain that reveals typical cluster of vessels/nidus (Fig. 7). AVMs often require assessment with DSA for better characterization and identification of associated aneurysms, and, to understand the flow-dynamics. DSA is also performed as an adjunct to embolization.

**DURAL ARTERIOVENOUS FISTULA**

Tentorial dural arteriovenous fistulas can cause a pattern of basilar hemorrhage that is indistinguishable from aneurysmal SAH. SAH and/or associated parenchymal bleed, however, can occur in other types of tentorial dural arteriovenous fistulas, especially those considered high-grade lesions (Borden II and III). These lesions are associated with cortical venous reflux/drainage. CTA/MRA may demonstrate venous sinus thrombosis and dilated, abnormal vessels. Conventional angiography is often needed, however, to diagnose and characterize the fistula and as an adjunct to plan endovascular therapy. A vast majority of these lesions lend themselves to endovascular embolization techniques.

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**Fig. 7.** Right occipital AVM presenting with acute convexity bleed on noncontrast CT (A). Nidus of serpiginous vessels on CTA (B) and axial T2-weighted image (C). CTA maximum intensity projections (D) and time-of-flight MRA (E) show predominant arterial supply of the AVM from right occipital and middle meningeal artery.
ISCHEMIC STROKE

Headaches occur in approximately 25% of patients with stroke and are more common with large ischemic stroke, in the territory of posterior circulation, in patients with migraine, and in younger patients. TCH presentation, however, is rare with stroke.

PITUITARY APOPLEXY

Hemorrhage or infarction of the pituitary gland rarely presents as TCH. This may occur with or without a known history of pituitary tumor. Pregnancy, general anesthesia, bromocriptine therapy, and pituitary irradiation are other known risk factors. These can easily be overlooked on CT and often detected and characterized on MR imaging (Fig. 8).

THIRD-VENTRICLE COLLOID CYST

Colloid cysts at the anterosuperior third ventricle can present with abrupt-onset headache that frequently is relieved by recumbency. Most are oval or rounded and situated at the foramen of Munro (Fig. 9). A majority are hyperdense on CT and hypointense on T2-weighted images, and 50% are hyperintense on T1-weighted images.

Fig. 8. A 30-year woman with TCH and noncontrast CT negative for SAH. MR imaging Sagittal T1 (A) and Coronal; T1-weighted (B) images show sellar heterogeneous, T1 hyperintense lesion with pituitary enlargement. Axial T2-weighted image (C) shows corresponding patchy low T2 signal. Follow-up Cor T1 (D) and T2-weighted (E) images done at 3 months and at 9 months (F, G) show progressive decrease in size and resolution of pituitary hemorrhage.
SUMMARY

TCH can have potentially catastrophic consequences and should be managed as a medical emergency. Initial assessment must be focused on excluding SAH. Imaging work-up depends on the time since onset of symptoms. Noncontrast CT is highly sensitive and specific in the first 6 hours to 12 hours. CSF evaluation by LP has high sensitivity when LP is done 12 hours to 2 weeks after SAH in patients with negative CT.96 LP is an invasive procedure, and some studies have proposed a CT/CTA algorithm to replace CT/LP.97 Utility of CTA, however, in this context is not established, especially given the incidental detection of intracranial aneurysms.34 This possibility should be discussed with patients before offering CTA, given the implication for subsequent aneurysmal treatment and/or imaging surveillance. MR imaging should be considered in patients with TCH who have negative CT and CSF analysis. CTA is sensitive for detection of intracranial aneurysm in patients with known SAH. In CTA-negative patients, further work-up should be decided based on the pattern of distribution of blood on CT. Repeat angiography should be considered in patients with aneurysmal SAH but may be of limited utility in perimesencephalic SAH.

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