



Subarachnoid Hemorrhage and Headache

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Published online: 23 May 2019

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Abstract

Purpose for Review Subarachnoid hemorrhage is a serious and life-threatening medical condition which commonly presents with an acute headache. Unfortunately, it remains frequently misdiagnosed at initial presentation with dire consequences in terms of patient morbidity and mortality. The goal of this paper is to review salient features in the clinical history, as well as recently developed clinical decision rules, which can help determine which patients warrant further investigation for subarachnoid hemorrhage when the initial presentation is that of an acute headache.

Recent Findings A recent prospective observational study showed that occipital location, stabbing quality, presence of meningism, and onset of headache during exertion were characteristics in the clinical history that can distinguish the headache of SAH from other causes. The Ottawa headache rule is a clinical decision tool which was developed to help identify patients presenting to the ED with acute non-traumatic headache who require investigation to rule out subarachnoid hemorrhage. Using this tool, it is recommended that patients who meet any one of the following 6 criteria are investigated further: Onset greater than or equal to 40 years, presence of neck pain or stiffness, witnessed loss of consciousness, onset during exertion, thunder clap headache (pain peaking within 1 s), or limited neck flexion on exam.

Summary An informed and thoughtful approach that takes into account the timing, presentation, risk factors, and resources, as discussed here, should help distinguish between the patient that warrants further evaluation and intervention for SAH and one who does not. The Ottawa SAH rule is a useful clinical decision tool for young inexperienced clinicians in order to avoid missed diagnoses. However, its clinical value is limited by its low specificity. Clinical decision tools with higher specificity are needed.

Keywords Subarachnoid hemorrhage · Clinical decision rules · Headache characteristics · Ottawa SAH rule

Introduction

Subarachnoid hemorrhage (SAH) is a serious life-threatening medical emergency that classically presents with a sudden-onset severe headache described by patients as the “worst headache of my life” [1]. The headache in-

tensity can be moderate and the key feature is the abrupt onset; therefore, the presence of any acute-onset headache regardless of severity or prior headache history should prompt at least a consideration of SAH [2]. The ICHD3 diagnostic criteria [3] for acute headache secondary to non-traumatic subarachnoid hemorrhage are as follows: (Table 1).

SAH often presents with other neurological symptoms and signs in addition to an acute headache including altered level of consciousness, cranial neuropathies, focal weakness, and meningism

In patients in whom focal neurological symptoms or signs are present, the diagnosis is often straightforward as the presence of an abnormal exam prompts immediate imaging. However, in patients in whom headache is the sole presenting symptom of SAH, missed diagnosis can be an issue. Studies have reported the frequency of misdiagnosis of SAH range from 12 to 51% [4–13].

This article is part of the Topical Collection on *Uncommon and/or Unusual Headaches and Syndromes*

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Table 1 ICHD 3 diagnostic criteria for acute headache attributed to non-traumatic subarachnoid hemorrhage

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- A. Any new headache fulfilling criteria C and D
- B. Subarachnoid hemorrhage in the absence of head trauma has been diagnosed
- C. Evidence of causation demonstrated by at least 2 of the following:
1. Headache has developed in closer temporal relationship to other symptoms or signs of SAH, or has led to the diagnosis of SAH
 2. Headache has significantly improved in parallel with stabilization or improvement in other symptoms, clinical or radiological signs of SAH
 3. Headache has sudden or thunderclap onset
- D. Either of the following:
1. Headache has resolved within 3 months
 2. Headache has not resolved but 3 months have not yet passed
- E. Not better accounted for by another ICHD-3 diagnosis**
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*In which the diagnosis is confirmed by CT and/or lumbar puncture. In the presence of non-traumatic convexal subarachnoid hemorrhage, older age, sensorimotor dysfunction, stereotyped aura-like spells, and absence of significant headache suggest cerebral amyloid angiopathy as the underlying cause while in younger patients with recurrent thunderclap headaches, this is more suggestive of reversible cerebral vasoconstriction syndrome (RCVS) as the primary cause

Initial misdiagnosis is more likely to occur in nonteaching hospitals [14]. In a cohort study of 482 patients admitted to a tertiary care urban hospital with SAH, multivariate analysis revealed normal mental status (Hunt-Hess grade I or II) at first medical contact and small volume of SAH were both independent predictors of misdiagnosis [4]. In this study, misdiagnosed patients were more likely to have died or be severely disabled at 3 and 12 months. Among survivors, misdiagnosed patients also had poorer quality of life scores [4]. It appears that the patients who are most likely to benefit from early treatment are the population most at risk of initial misdiagnosis and the consequences of diagnostic delay in terms of morbidity and mortality are high as evidenced by this study. Therefore, it is important to not miss the diagnosis in patients with a normal mental status. However, given that headache as a presenting complaint accounts for a large number of emergency department visits, it would be a waste of resources to suggest that every single patient presenting with a headache go on to have a head CT and or lumbar puncture to rule out SAH.

In this paper, we will review features in the clinical history, as well as recently developed clinical decision rules, which can help determine which patients warrant further investigation when the initial presentation is that of an acute headache.

Distinguishing Characteristics

SAH classically presents with a thunderclap headache which is defined as a severe headache of abrupt onset and reaching maximum intensity in less than 1 min [15]. The most common

causes of thunderclap headache are SAH and RCVS. However, there remains a wide range of etiologies that can present with a thunderclap headache [15–17] (see Table 2). While a thunderclap headache should always prompt a work-up, there are often additional specific clues in the clinical history that can help to narrow the differential diagnosis.

A prospective observational study in 2017 [18**] examined the clinical features of the presenting headache in people with SAH in the emergency department and neuro intensive care unit of a tertiary academic medical center. A total of 158 patients were enrolled of whom 20 patients had SAH and 138 patients did not. Notable distinguishing features found on clinical history in this population were headache located in the occipital region (55% in the SAH group vs 22% in the non SAH group $P < 0.001$), stabbing quality (35% in the SAH group vs 5% in non SAH group, $P < 0.001$), presence of prior headache (50% in the SAH group vs 83% in the non SAH group, $P = 0.002$), and presence of meningism (80% in the SAH group vs 42% in the non SAH group, $P = 0.002$). An additional historical feature which reached statistical significance was that 70% of the patients with SAH had a headache that began during exertion vs only 6% of the patients with an alternative diagnosis. In terms of the tempo of the headache of SAH, an interesting finding from this study was that the majority of patients with SAH had a headache which reached peak intensity within 1 s (instantaneously). This was the case in

Table 2 Causes of thunderclap headache [Adapted from 15, 16]

Most common causes of thunderclap headache
•Subarachnoid hemorrhage
•Reversible cerebral vasoconstriction syndrome (RCVS)
Less common causes of thunderclap headache
•Other intracranial hemorrhage
•Cervical artery dissection
•Cerebral venous sinus thrombosis
•Spontaneous intracranial hypotension
•Hypertensive crisis
•Posterior reversible leukoencephalopathy syndrome (PRES)
•Complicated sinusitis/meningitis
Uncommon causes of thunderclap headache
•Pituitary apoplexy
•Pheochromocytoma
•Aqueductal stenosis
•Third ventricle colloid cyst
•Pneumocephalus
•Retroclival hematoma
•Acute myocardial infarction [17]
Uncertain causes of thunderclap headache
•Primary thunderclap headache
•Unruptured intracranial aneurysm (sentinel headache)

65% of patients in the SAH group vs 10% in the non SAH group ($P < 0.001$).

As a brief aside, a common fallacy among non-neurologists/neurosurgeons is the misapprehension that a response to triptans is specific to the diagnosis of migraine and rules out secondary headaches such as SAH. This is not the case and there have been multiple case reports [19–22] of response to triptans in patients who were subsequently found to have subarachnoid hemorrhage. Triptans block transmission from the trigeminal nerve to second-order neurons in the trigeminal nucleus caudalis [19, 23]; therefore, any process that activates trigeminal nerve fibers including SAH, cluster headaches, meningitis, and migraine can be alleviated by the use of triptans. It is important to keep this in mind to avoid false reassurance and diagnostic errors.

Clinical Decision Rules

It is difficult to determine which patients who present with only headache and no neurological deficits warrant further investigation for SAH. Therefore, clinical decision rules have been developed to reduce uncertainty in medical decision making. They are derived from original research and can be defined as any decision-making tool which incorporates 3 or more variables in the clinical history, exam, or simple tests [24, 25]. The most studied clinical decision rule for SAH is the Ottawa SAH rule which has been prospectively validated [26].

It was developed to help identify patients presenting to the ED with acute non-traumatic headache who require investigation to rule out subarachnoid hemorrhage. Enrolled patients were 2131 adults over the age of 15 with a headache peaking within 1 h and a normal neurological exam. Exclusion criteria were the presence of new neurological deficits, prior aneurysms, prior SAH, known brain tumors, hydrocephalus, or chronic recurrent headaches (greater than or equal to 3 headaches of the same character and intensity for greater than 6 months).

The rule indicates a need for further investigation for SAH if one or more of the following 6 risk factors are met:

- Onset greater than or equal to 40 years
- Presence of neck pain or stiffness
- Witnessed loss of consciousness
- Onset during exertion
- Thunder clap headache (pain peaking within 1 s)
- Limited neck flexion on exam

It has a 100% sensitivity (95% CI 97.2%–100%) and 15.3% specificity (95% CI, 13.8%–16.9%) for identifying SAH in patients presenting to the ED with non-acute traumatic headaches. While it is a great rule out test given the 100%

sensitivity and should reduce the number of missed diagnosis if used, the low specificity means it is unlikely to reduce the number of unnecessary tests. A subsequent validation study by the same group in a new cohort of patients published in 2017 [27] showed similar sensitivity (100%) and specificity (13.6%) but also assessed the potential impact of the Ottawa SAH rule on neuroimaging rates in comparison to actual practice and showed a less than 5% decrease in diagnostic testing in the form of CT head + lumbar puncture. In this study, there was an 89% actual investigation rate versus 84.3% investigation rate if the Ottawa SAH rule had been followed.

An external retrospective validation study [28] was even worse, showing that in their patient population the use of the Ottawa SAH rule would have increased the rates of investigation with cranial CT or LP by 13%. In their cohort, 80% of patients underwent head CT or LP and no cases of SAH were missed during the usual course of patient care but application of the rule would have suggested further testing in 93% of patients suggesting that application of the rule could lead to an increase in unnecessary testing and health care costs without improving safety.

In addition, the specific inclusion and exclusion criteria for the Ottawa SAH rule meant that the rule could only be applied to a minority of ED patients with a headache (only 8.4% of patients presenting to the ED with a headache were eligible for the rule). The applicability to only a minority of patients in addition to its low specificity limits its clinical value.

A new clinical decision rule [29], the EMERALD (Emergency Medicine, Registry Analysis, Learning and Diagnosis) SAH rule was proposed in 2016 using only objectively measurable predictors to exclude SAH in order to offer higher specificity than the Ottawa SAH rule while maintaining similar sensitivity. This multicenter prospective study was conducted in the emergency departments of 5 general hospitals in Japan. A total of 1899 patients aged over 15 years with acute headache and presenting within 14 days of onset were considered for enrollment. Patients with headaches caused by trauma, drugs, or alcohol, those who were unconscious at the beginning of assessment, and patients with greater than or equal to 3 recurrent headaches with the same characteristics and intensity as the presenting headache over a period of greater than 6 months were excluded. A total of 1561 patients were enrolled and a new rule was developed. According to the rule, patients with any of the following measurements should receive imaging:

- Systolic blood pressure > 150 mmHg,
- Diastolic blood pressure > 90 mmHg,
- Blood sugar > 115 mg/dl (6.9 mmol/l), or
- Serum potassium < 3.9 mEq/L (3.9 mmol/l)

This new rule has a 100% sensitivity (95% CI 98.6% to 100%) and 14.5% specificity (95% CI 12.5% to 16.9%) which is similar to the Ottawa SAH rule. The authors propose that the Ottawa SAH rule should be used as the first screening step with the EMERALD rule being used as a second step to obtain higher specificity, thereby reducing unnecessary imaging. While a strength of the rule is the use of objective measures thereby reducing the chance of interobserver variation, drawbacks are that this rule has not been shown to offer higher specificity than the Ottawa SAH rule, venipuncture is necessary thereby introducing possible diagnostic delay while awaiting blood test results, it is not as clinically intuitive as the Ottawa SAH rule, and it has not been externally validated.

Conclusion

Of the secondary headaches (those due to another medical condition), SAH is among the most serious. In addition to the obvious medical consequences of under diagnosis, SAH is a powerful driver of excessive testing in the emergency room and, as consequence, the ballooning of cost of healthcare. Thus, for both medical and socioeconomic reasons, it behooves medical professionals to utilize the best tools available in assessing the patient who presents to the ED with an acute severe headache. While many patients with SAH may present with the combination of severe headache of rapid onset coupled with cranial nerve or other neurologic findings, including nuchal rigidity, a significant minority will present without these identifying characteristics, and indeed, it is these patients who are most frequently missed, with dire consequences.

The challenge of balancing the risks of a missed diagnosis against the costs of excessive, inappropriate workup is difficult. Certainly, when doubt exists, it is better to err on the side of medical safety. At the same time, an informed and thoughtful approach that takes into account the timing, presentation, risk factors, and resources, as discussed here, should help distinguish between the patient that warrants further evaluation and intervention for SAH and one who does not.

The Ottawa SAH rule is a useful clinical decision tool for young inexperienced clinicians in order to avoid missed diagnoses. However, its clinical value is too limited by its low specificity.

Compliance with Ethical Standards

Conflict of Interest Oyindamola Ikepo Ogunlaja and Robert Cowan declare no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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