African Journal of Emergency Medicine (2014) 4, 140–149

African Federation for Emergency Medicine

African Journal of Emergency Medicine

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CLINICAL REVIEW

The diagnosis of and emergent care for the patient with subarachnoid haemorrhage in resource-limited settings

Étude clinique : Le diagnostic et les soins d'urgence des patients souffrant d'hémorragie sous-arachnoïdienne dans des contextes caractérisés par des ressources limitées

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Received 25 June 2013; revised 31 March 2014; accepted 27 April 2014; available online 11 June 2014

Non-traumatic subarachnoid haemorrhage (SAH) is a neurosurgical emergency that may present similarly to a benign headache, yet poses high morbidity and mortality in what often times are young and otherwise healthy patients. While the diagnosis may be made via several different modalities, not all of these are available to every emergency physician. A high suspicion for SAH along with a good history and physical examination may best serve patients in these resource-limited settings. Adequate resuscitative and supportive care, combined with prompt transfer to a facility with neurosurgical capabilities is integral to optimizing patient outcomes.

L'hémorragie sous-arachnoïdienne (HSA) non traumatique est une urgence neurochirurgicale que l'on peut aisément confondre avec une méningée bénigne, mais qui est pourtant associée à de forts taux de morbidité et de mortalité chez des patients souvent jeunes et généralement en bonne santé. S'il est possible d'établir un diagnostic en suivant différentes modalités, celles-ci ne sont pas toutes à la disposition de tous les médecins urgentistes. De forts soupçons de HSA associés à un bon examen des antécédents et un bon examen physique constituent probablement la meilleure option pour les patients dans ces contextes caractérisés par des ressources limitées. Des soins de réanimation et de maintien, suivis d'un transfert rapide vers une structure dotée d'un service de neurochirurgie, sont essentiels pour optimiser l'état de santé des patients.

African relevance

- There is a dearth of epidemiologic research on the incidence, mortality, and economic impact of subarachnoid haemorrhage (SAH) in Africa.
- Diagnosis and management of SAH is challenging in resource-limited settings and requires less reliance on neuroimaging and early efforts for transfer to an institution with neurosurgical care.
- Several areas of controversy including seizure prophylaxis, blood pressure control, and antifibrinolytic therapy are aspects of management to discuss with the accepting physician at a transferring institution if possible.

Introduction and importance to Africa

Subarachnoid haemorrhage (SAH) can be secondary to trauma or due to non-traumatic, aneurysmal disease. The latter will be discussed exclusively here.

An idea of the basic incidence and mortality of SAH in Africa can be gleaned from the small, country-specific articles that are available. For example, in a recent Kenyan autopsy study, 2.1% of 134 deaths were due to subarachnoid haemorrhage and in a Nigerian stroke registry, 11.3% of strokes over a two year period were due to subarachnoid haemorrhage.[1,2] One study from Morocco suggests that the incidence or at least the detection of aneurysmal disease is rapidly increasing with 2 patients identified to have cerebral aneurysm in 1983 to 24 patients in 1999 at a specialty hospital.[3] The outcome of patients diagnosed with SAH was found in one study to vary little by geography and depends more on neurological grade, patient age, and amount of SAH rather than any treatment variations. This study examined data from 3567 patients

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Peer review under responsibility of African Federation for Emergency Medicine.

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http://dx.doi.org/10.1016/j.afjem.2014.04.002

between 1991 and 1997 worldwide and found a minimal variation in outcome based on geography. However, the only African country included in this study was South Africa.[4]

Another major difference in the clinical evaluation of SAH specific to African countries is the relative shortage of computed tomography (CT) scanners available to clinicians as compared to other clinical settings. Without CT scanners, healthcare providers must rely on history, physical exam, and lumbar puncture to make the diagnosis of SAH.

Between 1% and 4% of patients with headache reporting to the emergency centre in low to middle income countries are ultimately diagnosed with subarachnoid haemorrhage.[5] Between 3% and 26% of patients with SAH die prior to reaching the hospital and those who do arrive alive have a high likelihood of rapid deterioration and mortality rate of up to 33%.[6] Therefore, considering SAH in the differential diagnosis of every headache patient and having the knowledge to recognize when it is appropriate to initiate the diagnostic evaluation for SAH are important clinical skills for every emergency physician.

Patients with SAH that are initially misdiagnosed have been found to appear clinically well as opposed to their counterparts with SAH and altered level of consciousness, focal motor deficit, or have a severe headache with classically abrupt onset during exertion who are much more likely to be correctly diagnosed on initial presentation. The most common alternate diagnoses that patients are ultimately found to have SAH are initially given are: headache of unknown cause, migraine/cluster/tension headache, or meningitis/encephalitis. Jonathan Edlow MD asserts that the misdiagnosis of SAH stems from three recurring patterns of error, ''failure to appreciate the spectrum of clinical presentation, failure to understand the limitations of computed tomography (CT), and failure to perform and correctly interpret the results of lumbar puncture.''[7]

Pathophysiology

Subarachnoid haemorrhage is a type of stroke in which bleeding occurs in the subarachnoid space alone or in conjunction with bleeding elsewhere in the central nervous system. The haemorrhage is classified as either primary (non-traumatic) or secondary (traumatic). This is a clinically important distinction as treatment options and prognosis differ with the specific aetiology of the haemorrhage. Approximately 75% of SAH are primary and, of those, 74% are due to a ruptured aneurysm. Twenty percent of patients with one aneurysm will have a second. A non-traumatic aetiology of SAH, based either on history or aneurysmal distribution pattern on head CT requires further imaging, such as CT Angiography (CTA), to identify aneurysms that may be amenable to surgical or endovascular intervention. The majority of non-traumatic SAH without an aneurysm are idiopathic while a minority are due to more rare conditions including arteriovenous malformations (AVM), cerebral artery dissection, coagulopathies, moyamoya syndrome, mycotic aneurysms, neoplasms, pituitary apoplexy, vasculopathies, or use of sympathomimetic drugs, such as cocaine, methamphetamine or phenylephrine.[8]

The deleterious effects of SAH include direct damage to the brain by the haemorrhage and resultant mass effect as well as the inflammatory cascade it triggers. Cerebral blood flow and autoregulation are reduced, resulting in global brain ischaemia. This leads to increased intracranial pressure (ICP), decreased cerebral perfusion pressure (CPP), and the continued propagation of the inflammatory cascade resulting in increased permeability of the blood brain barrier.[9]

History

Subarachnoid haemorrhage can occur in any age group, but its highest incidence is amongst those aged 40 to 60 years old and it occurs in a 3:2 female to male ratio.[10] Multiple international studies have identified hypertension, cigarette smoking, alcoholism, and cocaine use as risk factors for SAH.[11] Patients with a history of prior aneurysmal haemorrhage have a 1–2% risk of recurrence per year.[12] Up to 20–50% of patients have a warning headache in the days or weeks before presenting with acute SAH. This is sometimes called a ''sentinel headache'' or ''sentinel bleed'' and is, as the name implies, thought to be due to a relatively small bleed from the offending aneurysm that warns of a more catastrophic haemorrhage to come. In these patients, the goal is to make the diagnosis and intervene before the catastrophic bleed occurs. It is important to ask patients about family history since 2% of patients with a first degree relative with a history of an aneurysm will develop the disease themselves. This risk is even greater if multiple family members have been diagnosed with an aneurysm or if there is a family of autosomal dominant polycystic kidney disease (ADPKD).[13]

Physical exam

Physical exam findings may vary widely with one study demonstrating most patients with SAH arriving to the emergency centre with a GCS of 15 (55%) and a Hunt and Hess score of less than 3 (35%).[15] Providers should keep in mind that as cited above, most patients with SAH will present awake and alert. See below for Hunt and Hess scoring. In any patient with headache, abnormal level of consciousness, or vomiting the physician should strongly consider the possibility of SAH. In the presence of high-risk features (Table 1), improvement in symptoms alone, spontaneously or in response to treatment, should not dissuade the physician from continuing to pursue the diagnosis of SAH.

In the unconscious patient, ocular haemorrhages may be the only physical exam finding indicating SAH as a cause of the altered level of consciousness. These ocular haemorrhages may be flame-shaped, subhyaloid, or vitreous and are thought to be due to venous obstruction from increased intracranial pressure in SAH.[16]

Excluding SAH with clinical decision rules

Perry et al. enrolled close to 2000 patients over five years in Canada to identify high risk characteristics of patients to develop a clinical decision rule to exclude patients from further work-up for SAH. They developed three different rules for adult patients with non-traumatic headaches whose intensity peaked within an hour of onset or were associated with syncope. The most applicable version of their clinical rules for Africa is the only one that does not include arrival by ambulance (Table 2).

Table 1 Risk factors for and clinical characteristics of SAH. SAH subarachnoid haemorrhage.[14]

Sudden, severe headache that reaches maximal intensity in seconds to minutes after onset
Acute headache after exertion (i.e. sex, exercise, heavy lifting)
Prior history of SAH or aneurysm
Family history of SAH, Ehlers–Danlos Type IV, ADPKD, aortic coarctation, or Marfan's syndrome
Severe hypertension
Previous vascular injuries/malformations involving extracranial vessels
Young, middle-aged patients (40–60 years old)

Table 2 Perry et al. clinical decision rule.[17]

Investigate patients for subarachnoid haemorrhage further if one or more variables present
1. Age > 40
2. Complaint of neck pain or stiffness
3. Witnessed loss of consciousness
4. Onset with exertion

In its original study, this rule had 100% sensitivity and 28.4–28.8% specificity. An external validation of this rule resulted in a sensitivity of 97.1% for exclusion of SAH and it is therefore likely a useful tool to help identify patients with sudden, severe headache who require no further work-up (including head CT) for SAH in resource challenged environments.[18]

Diagnosis of SAH and the importance of timing

Delineating the time of onset of symptoms is critically important in the diagnosis of SAH. As discussed in the sections below, the sensitivity of head CT in SAH is more sensitive early in a patient's course and degrades rapidly the farther away from symptom onset. This is in contrast to the detection of xanthochromia, which is usually not detected until 12 h after symptom onset. While it may be difficult in patients with altered mental status or severe headache to nail down the exact moment of symptom onset, it is critical in judging the sensitivity and specificity of the diagnostic tests discussed below.

Laboratory studies

Laboratory studies in general, add little to the diagnosis of SAH. Their main role is to exclude other causes of serious headache including pre-eclampsia with proteinuria and a positive urine pregnancy test, meningitis or intracranial abscess which may have a leukocytosis on complete blood count, or cocaine-induced intracranial haemorrhage which may be seen on urine drug screen. Once the diagnosis of SAH is made, there are electrolyte derangements such as hypernatremia and hyperglycaemia that are common in SAH and their management is discussed later.

Radiology studies

A non-contrast head CT is an accepted routine part of the work-up of SAH (Figure 1), when available, but retrospective reviews have suggested 9% of SAH would be missed if the diagnostic algorithm relied on head CT alone. The diagnostic

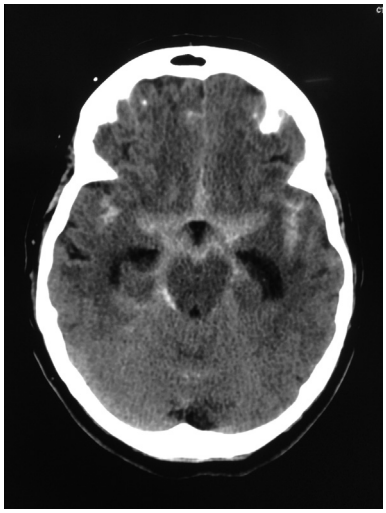

Figure 1 An example of the classic "starman" of subarachnoid blood that can be seen on a non-contrast head CT. This scan also shows early hydrocephalus with dilation of the temporal horns of the lateral ventricles, which can be present even after the acute SAH blood becomes isodense and is no longer distinguishable from brain tissue. Photo courtesy: Alex Koyfman, MD.

accuracy of CT can be affected by a number of factors including the patient's haematocrit, the time from the onset of symptoms to the acquisition of the CT images, the technical specifications of the scanner, and the skill of the person interpreting the scan.[19] A conservative estimate is that a patient's serum haematocrit needs to be at least 30% to distinguish blood from cortex on head CT (though some authors argue that this distinction can be made at levels as low as 27%).[20]

Images obtained from fifth generation CT scanners, completed within 6 h of symptom onset, and interpreted by a neuroradiologist have been reported to have 100% sensitivity for detection of SAH. Sensitivity drops to 85.7% in patients whose scans were done greater than 6 h after symptom onset as erythrocytes dissipate and lyse to an extent that it is difficult to distinguish them from the surrounding brain tissue after this time point.[21] The sensitivity of 100% for head CT performed within 6 h was validated at an additional facility over a 7-year period, but the investigators excluded SAH patients who presented without headache.[22] The interpreting radiologist also plays an important role in the sensitivity of CT. Scans read in non-tertiary centres by non-neuroradiologists carry a lower negative predictive value and, in one study in the Netherlands, 13% of CT scans read as negative in the local community were overread at a tertiary centre as positive or inconclusive for SAH. This decreased sensitivity based on the interpreting

radiologist is especially important to consider in African hospitals that do not have access to a neuroradiologist.[23] This sensitivity of CT scans obtained within 6 h has been contested by a retrospective case-control study that found a sensitivity of only 80%, with 11 of 55 subarachnoid haemorrhages detected to have negative head CTs and positive lumbar punctures.[24] It has been argued that this study by Mark et al. was limited in its retrospective nature, inclusion of patients with clear cranial nerve deficits, and mixture of both neuroradiologists and general radiologists interpreting the head CTs.[25]

For this reason, in the patient with a negative head CT or in facilities where head CT is unavailable, the patient should undergo lumbar puncture, except in cases noted above (symptom onset less than six hours with fifth generation CT scanner, and interpreted by a neuroradiologist) looking for the sequelae of haemorrhage in the subarachnoid space in the form of either red blood cells (RBCs) or their breakdown products of bilirubin and oxyhaemoglobin expressed as xanthochromia.[26]

However, there is debate about which patients need neuroimaging prior to lumbar puncture. The concern is that lumbar puncture may precipitate brain herniation in patients with elevated intracranial pressure due to a mass lesion. The published research is conflicting, but in general the patients at highest risk for deterioration after LP are those with impaired consciousness, a focal neurologic deficit, or clinical features of increased ICP. In the absence of any of these features, it is probably safe to proceed directly to LP when CT is not available.[27–30]

It has been a conventional teaching that visualizing venous pulsations ensures a normal ICP and that it is safe to perform a lumbar puncture in the absence of neuroimaging. To our knowledge, there is no study that confirms or denies this teaching. One study used advanced ophthalmologic techniques to compare central retinal vein pressures and ICP and found a direct correlation between the two although this study did not examine venous pulsations directly, but extrapolated in their conclusions that increased pressures would eradicate venous pulsations.[31] However, there are case reports of patients with documented venous pulsations found to have increased ICPs on lumbar puncture although none had acute neurologic changes after the procedure suggesting any herniation suggesting the presence of venous pulsations may still be an indicator of safety for lumbar puncture rather than an indicator of a normal ICP.[32]

The American College of Emergency Physicians (ACEP) has a clinical policy statement that endorses the use of lumbar puncture if head CT is an unavailable resource. This policy states, ''When subarachnoid haemorrhage is suspected, it is appropriate to perform a head CT and if negative, proceed to LP. If head CT is not readily available, selected patients may have diagnosis and care expedited with performance of an LP first. These patients should have no signs of increased intracranial pressure and no focal neurologic findings. In cases of negative LP and negative CT and high suspicion of aneurysm or AVM, other neuroimaging studies or consultation may be appropriate.''

Unfortunately, the diagnostic challenge does not end with the decision whether or not to obtain a head CT prior to lumbar puncture as the interpretation of CSF studies is not always straightforward. When performing a lumbar puncture to evaluate for SAH, one is looking specifically for the sequelae of bleeding in the subarachnoid space manifested by either xanthochromia or red blood cells (Figure 2). Xanthochromia is the yellowing of CSF as a result of bilirubin from the breakdown of erythrocytes and this enzyme-dependent process may take up to 12 h. Pink tinged CSF due to released haemoglobin from lysed red blood cells is detectable several hours sooner (See Table 3).

The reference standard for detecting xanthochromia is CSF spectrophotometry. However, most laboratories use simple gross inspection of the CSF looking for xanthochromia, which is much less sensitive and can miss the diagnosis in up to half of specimens when compared to spectrophotometry.[33,34] However, at least one study found a 100% sensitivity for detecting xanthochromia in CSF by clinicians, which may suggest that in resource-challenged settings xanthochromia may be excluded based on gross visual inspection alone. This same study found that if clinicians were unsure of the colour of CSF, describing it as ''doubtful'' than spectrophotometry was required to accurately exclude the presence of xanthochromia.[35] Xanthochromia itself, is not specific for SAH as it is also seen in clinical situations where CSF protein levels are high for other reasons such as various infections, inflammatory conditions, or traumatic taps that have $>100{,}000$ RBCs introduced into the subarachnoid space.[36]

The absence of red blood cells in clear CSF effectively excludes subarachnoid haemorrhage. When red blood cells are present in the CSF in the absence of xanthochromia, there are two primary possibilities: either the patient has a subarachnoid haemorrhage and there has been insufficient time from the onset of bleeding to allow for the development of xanthochromia or the CSF has been contaminated by red blood cells as a result of injury induced by the procedure itself (a ''traumatic tap''). The provider's impression of a traumatic lumbar puncture is subjective and prone to error.

Investigations of CSF D-dimer assays to differentiate SAH from a traumatic tap were initially promising, but subsequently found to be unhelpful and are not recommended to differentiate traumatic vs. RBCs from true SAH.[37,38]

Another method that has traditionally been used to differentiate true SAH from a traumatic tap is to compare the red blood cell count in the first CSF tube to that in the final tube. Indeed, while a decreasing red blood cell count is reassuring,

Figure 2 A clearly positive lumbar puncture performed on a patient with several days of apoplectic headache, a head CT only significant for mild early hydrocephalus, and a CTA positive for aneurysmal SAH. Photo courtesy of Michael Runyon, MD.

Table 3 Summaries of the Hunt and Hess Scale, the World Federation of Neurological Surgeons Scale, and the Prognosis on Admission of Aneurysmal Subarachnoid Hemorrhage Scale.[51–55]

Grade	Hunt and Hess Scale	WFNS Scale	PAASH Scale
I	Asymptomatic, or minimal headache and slight nuchal rigidity	GCS score 15	GCS score 15
II	Moderate to severe headache, nuchal rigidity, no neurological deficit other than cranial nerve palsy	GCS score 13–14 without focal deficit	GCS score 11–14
III	Drowsiness, confusion, or mild focal deficit	GCS score 13–14 with focal deficit	GCS score 8–10
IV	Stupor, moderate to severe hemiparesis, possibly early decerebrate rigidity, and vegetative disturbances	GCS score 7–12	GCS score 4–7
V	Deep coma, decerebrate rigidity, moribund appearance	GCS score 3–6	GCS score 3

especially if the count in the final tube approaches zero, no single absolute or percent decrease in CSF red blood cell count in subsequent specimen tubes has proved reliable for excluding the diagnosis of SAH.[39] A recent small retrospective study however may provide some guidance. Gorchynski et al. retrospectively looked at 305 patients with RBCs present in their CSF and found a negative predictive value of 100% for SAH on CT when the RBC count was less than 500 in the fourth CSF tube and a corresponding positive predictive value of 100% when the RBC count was greater than 10,000 in the fourth CSF tube.[40] A more recent and larger case series of close to 5000 patients who underwent lumbar puncture over an eight year period also found that the RBC count in the fourth tube was helpful in risk stratifying patients for SAH. This study found no patient with SAH who had less than 100 RBCs in the fourth tube of CSF while greater than 10,000 RBCs in the fourth tube increased the odds of SAH by a factor of 6.[41] While each study has its own limitations, these cell counts may help provide some guidance to physicians practicing in resource-limited settings.

The timing of lumbar puncture is an important factor in determining the utility of the test for diagnosing SAH. Xanthochromia may present as soon as 6 h after symptoms of headache begin; however, some argue that in a stable patient it may be reasonable to delay lumbar puncture for 12 h after symptom onset as sensitivity of the test approaches 100% at this time. Xanthochromia is still detectable in almost 100% of patients two weeks after haemorrhage, 70% after three weeks, and in 40% of patients after one month.[42,43]

Alternative management strategies include performing an immediate lumbar puncture and if the tap is non-diagnostic in a patient with a high risk features for SAH, repeat the procedure at 12 h after symptom onset to maximize sensitivity and avoid unnecessary transfers.[44]

Researchers have also attempted to delineate when it is safe to forgo CT all together and utilize lumbar puncture alone to rule out SAH. Schull found that 8–12% of patients complaining of headache with a onset of less than one minute and normal neurologic exam, normal vital signs including temperature, normal level of consciousness, and no neck stiffness. Lumbar punctures performed at 12 h after symptom onset in his patient population were close to 100% sensitive for SAH when spectrophotometry was performed looking for xanthochromia. However, this may not apply to settings with a higher prevalence of HIV. This high sensitivity of delayed lumbar puncture may be especially useful in settings with limited availability to CT scanners. Schull constructed mathematical models based on a proposed algorithm of waiting until 12 h after symptom onset to perform LP the above patient population and if negative, to discharge them home effectively having ruled out the diagnosis of SAH (Figures 3 and 4). Patients with indeterminate or positive LPs underwent head CT. In this mathematical model, out of 100 patients who underwent this "LP first" model, there would be 79–83 fewer head CTs performed and 7–11 additional LP's performed. This study had several limitations including the fact that it was a theoretical model and has not been part of a clinical trial, but does provide evidence that a prospective study of this "LP first" model may help decrease unnecessary diagnostic radiation exposure and could prove beneficial in settings where CT imaging is not accessible.[45]

In clinical settings where more advanced radiography is available, CT angiography has been considered as a possibility for looking directly at the cerebral vasculature for an aneurysm. CTA consistently has 100% sensitivity for larger aneurysms, but this drops off and is as low as 92% in aneurysms less than 4 mm.[46,47] It is important to note that approximately 2% of the population will have an asymptomatic cerebral aneurysm detectable on CT angiography.[48] The main question at the time of evaluation is not whether the patient has an aneurysm, but whether they have subarachnoid haemorrhage. Detection of an incidental aneurysm puts the patient at risk for potentially unnecessary interventions such as aneurysmal coiling or clipping and the potential complications of those interventions. The CTA itself also increases the risk of malignancy secondary to radiation exposure and renal injury from the nephrotoxic effects of contrast.[49] There is also a significant psychological burden placed on a patient if he or she knows they have a cerebral aneurysm which may unnecessarily increase anxiety surrounding any future headaches or head trauma. Another risk of moving towards CTA as a primary diagnostic tool in SAH is the concept of "technology creep" or the skills of physicians as diagnosticians will be lost to increasing rates of radiographic imaging in patient work ups.[50]

Management

Once the diagnosis of SAH has been made, grading the severity of the bleed and clinical condition of the patient via one of the numerous clinical grading systems facilitates communication of the patient's clinical status and likely prognosis between physicians and provides a reproducible method of ongoing

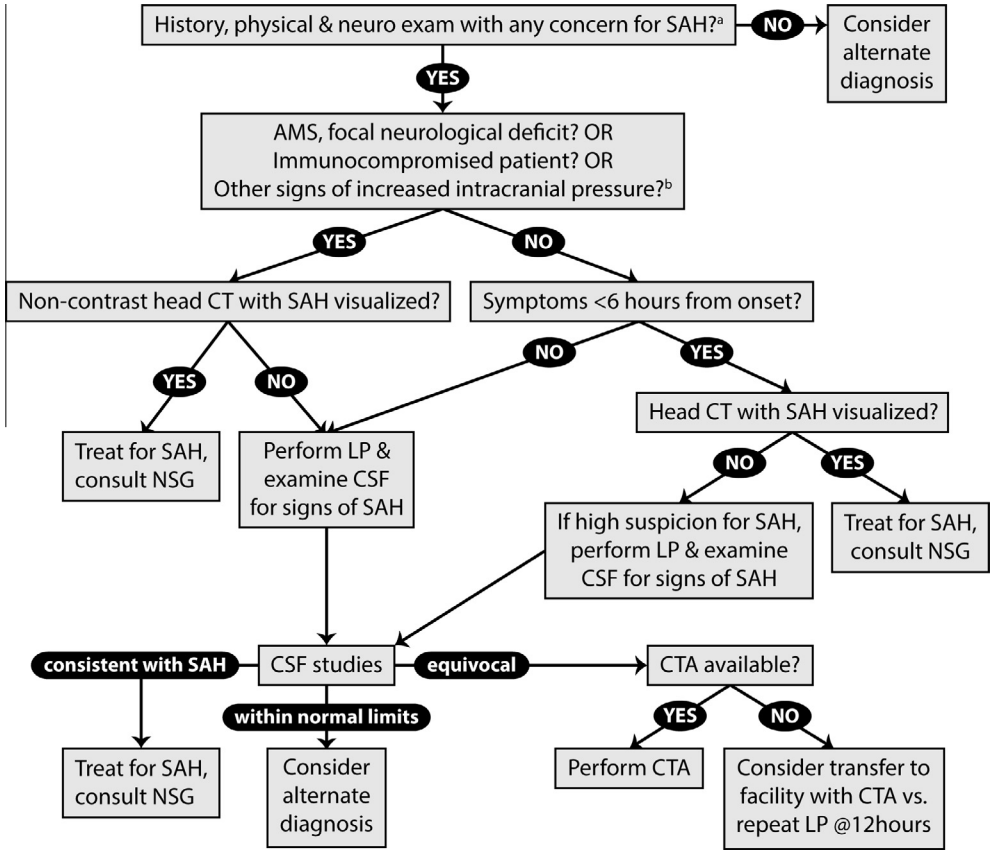

Figure 3 Possible diagnostic algorithm for SAH in resource limited ED where non-contrast head CT is available. AMS = altered mental status, CT = computed tomography, CTA = computed tomography angiography, LP = lumbar puncture, LOC = level of consciousness, NSG = neurosurgery, SAH = subarachnoid haemorrhage, Tx = transfer. [a]Refer to Tables 1 and 2. [b]Unilaterally dilated pupil, hypertension with bradycardia, persistent vomiting.

monitoring for clinical deterioration. Several different scales have been developed including the Hunt and Hess Scale,[51] Glasgow Coma Scale,[52] Fisher Scale,[53] Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage (PAASH)[54] and World Federation of Neurological Surgeons Scale (WFNS)[55] The Hunt and Hess Scale and WFNS are among the most commonly used. In a cohort of 50 patients with confirmed SAH, the interobserver variability was found to be highest in the Hunt and Hess scoring system and lowest in the WFNS and PAASH scales.[56] In a previous study of 537 patients with SAH, the prognostic value of the WFNS and PAASH were compared with PAASH being slightly favoured as its odds ratio for poor outcome at three months increased more gradually than that of the WFNS.[57]

While the optimal end points for blood pressure management remain controversial, there is some evidence that re-bleeding is more common in patients with a systolic blood pressure of greater than 160 mmHg and this complication worsens the overall prognosis.[58] Ideal agents to control a patient's blood pressure in SAH include nicardipine, labetalol, and esmolol, rather than the non-selective vasodilators nitroprusside or hydralazine which can theoretically increase ICP.

Ischaemia due to vasospasm is a main threat to patients surviving the initial SAH. While the pathophysiology of vasospasm is not completely understood, it manifests as delayed cerebral ischaemia (DCI) and is radiographically apparent 5–15 days after the initial SAH. Nimodipine is a calcium channel antagonist that is predominantly a cerebrovascular dilator shown to have a long-lasting effect when applied topically or systemically and is thus far the only known agent with proven benefit against DCI.[59]

A 2008 literature review published in *Stroke* reconfirmed these findings and recommended oral nimodipine 60 mg every 4 h for three weeks as standard treatment of aneurysmal subarachnoid haemorrhage. It is still unclear what role, if any, other calcium channel blockers or those given by IV route have in the management of SAH for the prevention of vasospasm.[60] Oral nimodipine 60 mg every four hours is now a Class I recommendation for all patients diagnosed with SAH.

Magnesium sulphate has also been recently investigated as an agent to help decrease the incidence and severity of vasospasm and subsequent ischaemic disease in SAH. In a 2010 study in Germany, 107 patients with known SAH were randomized to either placebo or a bolus and drip of magnesium with serum target concentration of 2–2.5 mmol/L magnesium for up to 10 days followed by 12 days of oral therapy. The incidence of DCI was found to be lower in the magnesium vs. placebo group (22% vs. 51%) as measured by serial CT. Vasospasm was also lower in the magnesium group vs. placebo (67% vs. 85%).[61] However, a larger phase III study randomized 1204 patients to either magnesium or placebo for 20 days and found a lack of clinical benefit, even when subgroups were

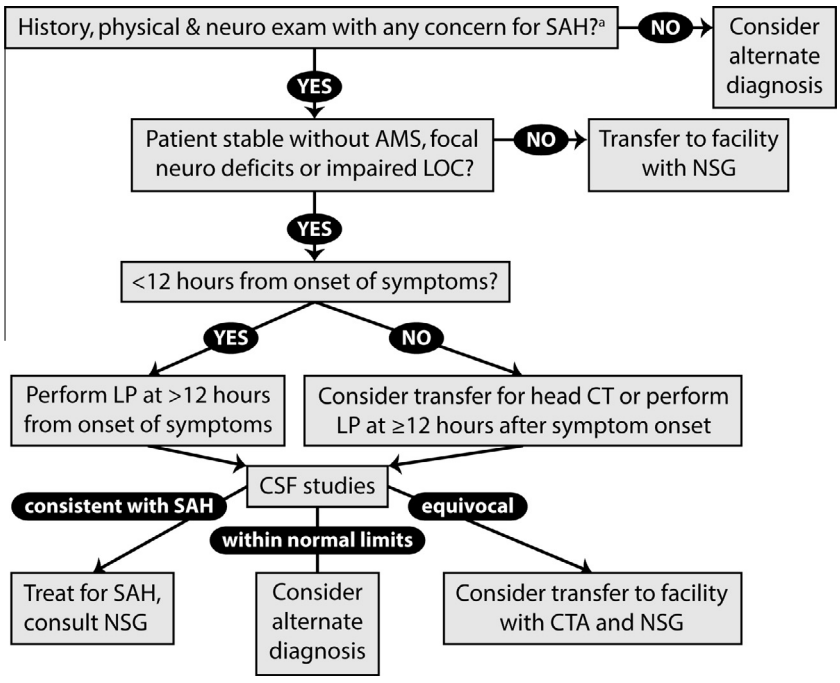

Figure 4 Possible diagnostic algorithm for SAH in resource limited ED where non-contrast head CT is not available. AMS = altered mental status, CT = computed tomography, CTA = computed tomography angiography, LP = lumbar puncture, LOC = level of consciousness, NSG = neurosurgery, SAH = subarachnoid haemorrhage, Tx = transfer. [a]Refer to Tables 1 and 2.

examined. This second study calls into question the utility of magnesium for preventing vasospasm in SAH.[62]

In addition to delayed ischaemia, re-bleeding is also a leading cause of morbidity and mortality in patients who initially survive SAH. Antifibrinolytic therapy to prevent re-bleeding in SAH has been studied since 1967, but still does not have a definitive role or strong recommendation in SAH treatment. In general, studies have suggested that the antifibrinolytic properties of agents such as tranexamic acid (TXA) or epsilon aminocaproic acid (EACA) may be offset by their detrimental side effect of cerebral vasospasm with resulting ischaemia.[63,64] There may be a role for TXA or EACA in the prevention of early re-bleeding in SAH if combined with early aneurysmal treatment such as surgical excision or clipping and prophylactic prevention of cerebral vasospasm concomitantly with these agents. One randomized prospective study of 505 patients with SAH did show a reduction in re-bleeding from 10.8% to 2.4% and an 80% reduction in mortality in patients receiving early TXA (1 g IV at time of CT diagnosis and then every 6 h until the aneurysm was occluded) as opposed to control patients with no apparent increased risk of ischaemic events or clinically significant vasospasm.[65] The most recent AHA guidelines offer a level IIa recommendation, ''For patients with an unavoidable delay in obliteration of aneurysm, a significant risk of re-bleeding, and no compelling medical contraindications, short-term (< 72 h) therapy with tranexamic acid or aminocaproic acid is reasonable to reduce the risk of early aneurysm re-bleeding.''[66] More prospective randomized trials will need to be performed to better elucidate any overall mortality benefit with this therapy and the duration of administration needed to maximize benefit while also limiting risk of cerebral ischaemia.

In addition to re-bleeding, hydrocephalus (defined as acute ventricular enlargement in the first 72 h) is another early complication of SAH, which is often associated with intraventricular extension of the bleeding. Hydrocephalus is seen in roughly 20–30% of SAH patients. The significance of hydrocephalus, is unclear in asymptomatic patients. If patients are symptomatic or have an altered level of consciousness, temporary or permanent diversion of cerebrospinal fluid (CSF) via ventriculostomy or shunt placement is recommended. Another option for the emergent shunting of CSF in the ED is lumbar puncture. This has the advantage of being a familiar and accessible procedure for the emergency physician, but has not been formally studied. The potential downside of this approach is that drainage of CSF via lumbar puncture prior to repair could potentially precipitate aneurysm rupture. However, it is reasonable to discuss this option with the consulting neurosurgeon as a potential temporizing measure in symptomatic patients.

The incidence of seizure and the role of prophylactic anticonvulsants in the management of SAH have not been well defined. Most studies looking at the incidence of seizure in SAH are retrospective and are not always able to clearly confirm the diagnosis of seizure activity since the reported events often occur in the pre-hospital setting or without EEG confirmation. In general, the prophylactic use of anticonvulsants, such as phenytoin, may be considered in the setting of acute SAH patient, especially if the patient has a history of prior seizure, but cannot be routinely recommended since the benefits of treatment are unclear. Some smaller retrospective reviews have actually reported a worse cognitive outcome at 3 months in patients loaded with phenytoin and a 23% incidence of adverse drug reaction secondary to anticonvulsant administration.[67–69]

Hyponatremia occurs in approximately 10–30% of patients with SAH and may predict worse clinical outcome. In uncontrolled prospective studies there was an association between hyponatremia and excessive natriuresis with volume

contraction, resulting symptomatic vasospasm, and downstream ischaemic effects. The natural response would be to replace this fluid with isotonic IV solutions, yet several studies have suggested fluid replacement with smaller volumes of hypertonic solutions such as 3% saline, 5% albumin, or treatment with mineralocorticoids, allow for smaller volume resuscitation, increased regional cerebral blood flow, increased brain tissue oxygen, and improved sodium levels vs. isotonic fluid replacement.[70] In general, the fluid status of patients with SAH needs to be closely monitored with invasive strategies such as CVP monitoring or daily weights in select patients when available.[71–73]

In addition to sodium, glucose control may also impact long-term outcome in SAH. A systematic literature search on glycaemic control in patients with SAH found 22 publications. Although individual studies varied, in general, presentation of SAH with hyperglycaemia was linked to worse outcome, but tight glucose control with insulin was associated with an increased risk of hypoglycaemia, which also was linked to worse outcome. This review concluded that while hyperglycaemia and hypoglycaemia should be avoided in SAH, there is not a specific glucose target in the management of SAH that can be recommended.[74]

As with any critically ill patient, maintenance of euthermia will help to decrease the systemic inflammatory cascade and so close temperature monitoring is appropriate in the emergency department

Ideally, all patients with known or suspected aneurysmal subarachnoid haemorrhage should have a neurosurgical consult to help define the optimal management strategy. This may involve stabilizing and transferring the patient to an alternative institution for definitive therapy, which is typically endovascular coiling or surgical clipping of the aneurysm. Patients with aneurysmal subarachnoid haemorrhage also will often undergo further diagnostic imaging to rule out a second aneurysm that has not yet ruptured. Specific recommendations from the AHA help guide screening in patient's asymptomatic relatives as the odds ratio of having an asymptomatic aneurysm in an individual with a first degree relative with aneurysm is 4.0.[75]

Disposition

When and where possible, all patients with SAH should be admitted to a neurosurgical intensive care unit for close monitoring. If neurosurgical consult is a significant distance from the current facility or the patient is clinically decompensating, consider pre-emptively securing the airway with endotracheal intubation prior to transfer if a ventilator or personnel who can manually ventilate throughout transport and upon arrival to the transferring facility are available. Also try to ensure that the transporting team has both the resources and training to closely monitor the patient's hemodynamic and neurologic status and intervene as indicated in the case of decompensation.

Conclusion

The exact incidence of SAH in Africa is unknown, but there is a suggestion it may be increasing in frequency and must be considered in any patient with a headache. SAH should be ruled out early in the patient's presentation as it carries a risk of rapid deterioration and high mortality. Several historical features including sudden severe pain after exertion, family history, and severe hypertension may aid in making the diagnosis and a normal neurological exam should not reassure the physician if the suspicion for SAH is high. If a patient has a normal head CT, but symptoms began greater than 6 h prior to the study a lumbar puncture should be performed to look for evidence of blood in the cerebrospinal fluid (CSF). Once the diagnosis of SAH is made, early arrangement for a facility with neurosurgical capabilities is paramount. Prior to transfer, patients should undergo standard resuscitation with close monitoring for change in clinical condition. Blood pressure control, electrolyte monitoring, and temperature management are all critical in the emergency department. Discussions regarding antifibrinolytic therapy with either tranexamic acid (TXA) or epsilon aminocaproic acid (EACA) as well as seizure prophylaxis with anti-epileptics and management of hydrocephalus via CSF drainage should all be mentioned with the accepting neurosurgeon. All patients with SAH should be admitted to a neurosurgical intensive care unit for either endovascular coiling or surgical clipping for definitive management of the aneurysm.

Conflicts of interest

The authors declare no conflict of interest.

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